THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

MARCH, 1906.

SPECIAL ARTICLE.

LATE RESULTS OF THE TREATMENT OF INOPERABLE SARCOMA BY THE MIXED TOXINS OF ERYSIPELAS AND BACILLUS PRODIGIOSUS.

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In September, 1891, in an article entitled "A Contribution to the Knowledge of Sarcoma," published in the *Annals of Surgery,* I reported three cases of inoperable sarcoma treated by repeated injections of the streptococcus of erysipelas. In my study of the cases of sarcoma treated at the New York Hospital during the preceding fifteen years, I had found one case of very malignant round-celled sarcoma of the neck, four times recurrent, in which an attack of erysipelas had accidentally occurred shortly after the last operation by Dr. Bull. At this time the tumor so extensively involved the deeper tissues of the neck that no attempt was made to remove it. A few days after the first attack of erysipelas had subsided, a second attack followed, lasting for a week. During these attacks of erysipelas the tumor of the neck entirely disappeared and the patient left the hospital in good health. After great effort I finally succeeded in tracing the after-history of this patient and found him alive and well in 1891, seven years later.

At this time I had not read of the experiments of Fehleisen in inoculating malignant tumors with the streptococcus of erysipelas, but was sufficiently impressed by the foregoing case to undertake a series of investigations. It so happened that Dr. William

T. Bull then had a patient with inoperable, recurrent spindle-celled sarcoma of the tonsil and glands of the neck, who was in such a hopeless condition that he was willing to try anything in the way of an experiment. Dr. Bull very kindly gave his endorsement. I worked for four months during the summer of 1891 vainly attempting to produce erysipelas by inoculation. After trying cultures from three different laboratories, I finally succeeded, however, with a culture kindly brought me by Dr. F. Ferguson from Koch's laboratory. The attack was very severe. I injected seven minims of a fluid bouillon culture beneath the skin over the tumor of the neck. In one hour there was a severe chill lasting forty minutes, followed by nausea and vomiting; the temperature rose to 105° and in twelve hours there developed a typical attack of erysipelas which gradually spread over the entire face and head. The attack subsided in about ten days. The changes in the tumor were most striking. The tumor of the neck became paler and much softer, and began to break down with a free discharge of caseous material on the second day; this continued for ten days. The outlying nodules disappeared without breaking down and the tonsil tumor decreased in size. At the end of two weeks the tumor of the neck had disappeared entirely. The patient's appetite returned and he gradually regained his lost weight, in fact, became perfectly well with exception of his previously contracted morphine habit. The tonsil tumor never disappeared, but remained as a hard, fibrous mass, apparently having lost its malignant character. The patient continued well for eight years, when there was a local recurrence which proved fatal not long after.

I have described this case somewhat fully, for upon it is based all of my subsequent work. Within the following year, with the valuable coöperation of Dr. Bull, I was able to treat nine other cases with the living cultures of erysipelas streptococcus.[1] There were no deaths in this series, although I had two fatal cases not long after. All of these cases were, of course, inoperable and quite hopeless. Four were carcinoma and six sarcoma.[2] The results, in brief, were as follows:

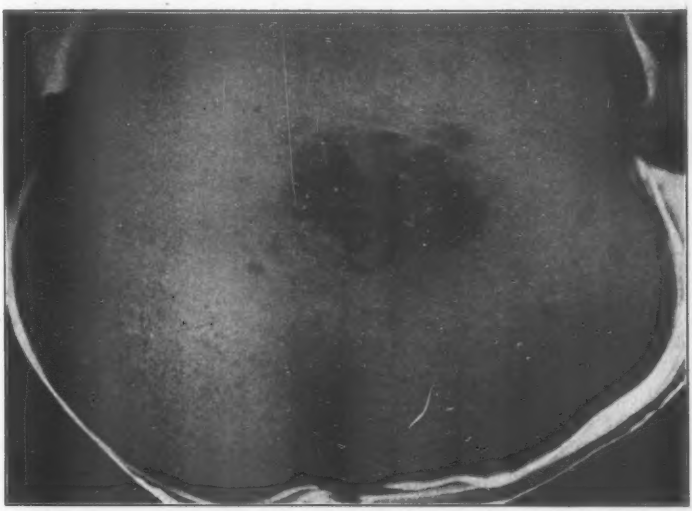
In six cases I was unable to produce erysipelas, although frequent injections with fluid cultures were made for many weeks. In none of the cases of carcinoma was an actual attack of erysipelas produced, but in most cases there was slight improvement in the local condition while the patient was receiving these repeated injections with the fluid cultures. Of the six cases of sarcoma inoculation was successful in only four. In the cases in which it was impossible to produce an attack of erysipelas—as in carcinoma

[1] These cases were treated in a special building, erected for the purpose, at the General Memorial Hospital, and donated by Mr. Archer M. Huntington.

[2] Published in the AMERICAN JOURNAL OF THE MEDICAL SCIENCES, Feb., 1893.

—there was slight, but always temporary improvement. Two of the cases were extensive bone sarcomas, one of the femur and one of the dorsal spine, both of very rapid growth. Of the four cases in which inoculation was successful and an attack of erysipelas ensued, one was the case already described, with sarcoma of the neck and tonsil in which the patient remained well for eight years and then died of recurrence. Case II. was a very extensive, inoperable, mixed, round-oval and spindle-celled sarcoma of the back and groin. This patient was inoculated on April 21, 1892. Repeated daily injections with the living cul-

FIG. 1



Sarcoma of back and groin. Mixed-celled. Disappeared under attacks of erysipelas. (Inoculation.) Recurred. Again disappeared under toxins. Well 3½ years. Died later. Abdominal metastases. See Case II.

tures of the streptococcus of erysipelas, obtained from the laboratory (of the College of Physicians and Surgeons), were given for three weeks without producing an attack. In the beginning of the fourth week injections of 20 minims of new cultures from Johns Hopkins Hospital were tried. After the second injection of 20 minims of bouillon culture there was a very severe chill, quickly followed by nausea, vomiting and a temperature of 105.5°. The attack lasted for ten days. The changes in the tumor in this case were even more striking than in the first. Within the first twenty-four hours of the attack, the glossy, bright red color of the tumor had become dull and lustreless, and the tumor itself

had shrunk considerably in size. On the second day a sinus formed, with free discharge of caseous, broken-down tumor tissue. A few days later the large, solid tumor in the groin, the size of a goose egg, also softened and broke down in the same way. (The area of erysipelas had not extended into the region of the groin.) The discharge continued for two weeks, at the end of which time there was bright granulation tissue in the region of the sinus, which quickly healed. At the end of three weeks there was no trace of tumor remaining either in the back or groin. Part of the primary tumor of the back had been removed before treatment and examination by Dr. F. Ferguson, Pathologist to the New York Hospital, and later by many other well-known pathologists, confirmed the diagnosis of mixed-celled sarcoma, the round cells predominating. Four weeks later the patient developed a localized abscess in the right pleural cavity, involving the lung, as shown by expectoration of a large amount of pus. An incision was made under cocaine and about a pint of pus evacuated and the sinus closed at the end of three weeks. The patient quickly regained his normal weight and strength. On the 1st of July, about three months later, there was a well-marked local recurrence in the back. On July 18th, several small nodules had appeared in an area of the back 2x4 inches. These grew rapidly. The injections of the fluid cultures were again begun and a tumor 7-8 inches in diameter, disappeared under repeated injections *without* any attack of erysipelas. Repeated attempts were made to produce erysipelas, without success, until November 14th, at which time there was an area of tumors 5x3½ inches and ½ to ¾ inches thick. During this interval the tumors would decrease in size, and some of them disappear under injections of large doses of cultures, but would grow again more rapidly as soon as the injections were discontinued. On November 14th, an injection of twenty-two minims of a culture which had been frequently used before, induced an attack of erysipelas, followed by a temperature of 105° and lasting for a week. The same changes took place in this instance as have already been recorded after the first attack. The tumors again entirely disappeared, both in the back and groin. Three weeks later, there was a second recurrence. During the following months three further attacks of erysipelas occurred spontaneously, although they were much milder in character than the two produced by inoculation. This patient finally fully recovered under injections of the mixed toxins, and remained well for three and one-half years, when he developed metastasis in the liver and abdomen.

Two very important facts were learned from the experience based on ten cases; *first,* that it is extremely difficult to produce erysipelas at will, and, *second,* that the curative properties of erysipelas are derived, in a measure at least, from the toxic prin-

ciples of the streptococcus, that might, hence, be utilized without an actual attack of erysipelas.

In addition to these facts, the danger of artificially produced erysipelas was strongly emphasized a short time afterward by two fatal cases. This, more than anything else, led me to attempt to utilize the toxins of streptococcus instead of the living germ. I began my experiments in 1892. At first I tried sterilization of fluid bouillon cultures by just sufficient heat to destroy the germs, 58° C., and also by filtering through a porcelain filter. In December, 1892, I first used the erysipelas toxins prepared in this way in four cases of inoperable sarcoma, making the injections directly into the tumor, and repeating same every forty-eight hours. The local and constitutional reaction was almost the same as in the case of a true erysipelas of mild degree, the symptoms always subsiding in twenty-four to forty-eight hours. The temperature never rose above 103.5°, and usually dropped to normal the following day. The filtered toxins were prepared for me by Dr. Alexander Lambert, of New York.

In order to intensify the action of the streptococcus of erysipelas, I began about this time using the combined toxins of bacillus prodigiosus and streptococcus of erysipelas. (Prepared for me by Dr. B. H. Buxton.) The idea was obtained from Rogers' then recent experiments upon rabbits. Different preparations of the toxins were made; in some, sterilization was done by filtration. The filtered toxins having been found to be very much weaker, and the beneficial results apparently less marked than those obtained with the unfiltered product, they were soon given up.

The Action of the Toxins. In my earlier paper already cited (American Journal of the Medical Sciences, 1893), I ventured an explanation of the curative action of the toxins, which seemed to my own mind, the most satisfactory. It rested upon the assumption that cancer (in which term I include sarcoma and carcinoma), is due to an extrinsic cause, or causes, or the presence of some micro-organism. While during the twelve years that have passed, no definite facts have been brought forth to positively prove this assumption, a much larger clinical knowledge of malignant tumors has served to convince me of the correctness of this theory. Most of the early objections to the parasitic origin of cancer have been answered by the discovery of new facts. Cancer has been proven to be more or less endemic. The researches of Guilliott have apparently proven it to be mildly contagious in man. Recent observations have shown conclusively that it is contagious in animals. We have recently proven that it can be easily transmitted from one animal to another by inoculations from the same species. The most significant fact is that successful inoculations of carcinoma have been made in mice with tumor tissues kept for long periods of time, in some

instances, in Ehrlich's laboratory, for more than a year. It is hardly conceivable that a living carcinoma cell, even when kept at a very low temperature, should retain its vitality for such a period of time, while it is quite in harmony with our knowledge of germs that a micro-organism should be able to live under such conditions.

Assuming then, for the moment, that malignant tumors are of micro-parasitic origin, this is the explanation I offered at the time: If a small quantity of blood serum of an animal rendered immune to tetanus is capable of destroying or rendering inert the virulent bacilli in a fresh case, it is quite as easy to understand that the toxic products of the erysipelas streptococci might bring about such changes in the blood serum as to destroy the parasite of cancer, or inhibit the growth. The parasite having been destroyed, the irritation would consequently cease, and this would lessen the hyperæmia of the parts, upon which factor the life of the tumor cells of low vitality largely depends.

The question may very properly be asked, why it is that the results are so variable, that some cases yield such brilliant results while others are apparently but little benefited by the toxins?

My own explanation is, that in all cases there is a certain balance of forces, the powerful proliferating tendency of the tumor cells on the one hand, the natural resisting power of the normal cells, aided by the blood serum, on the other. In certain cases, the toxins working through the blood serum, may so increase its normal resisting or destructive properties, that it more than counterbalances the proliferating forces of the tumor cells, and then we have retrograde changes, often ending in permanent cures. In certain other cases this action may only equal the latter, and then we have for a time cessation of growth or a state of equilibrium, until at length the one side or the other gains the ascendency. Finally, in other and, unfortunately, the majority of cases, the action of the toxins is never equal to the task, and while retardation of growth may occur, the tumor continues its course and eventually destroys life.

The same problem confronts us in explaining the action of the X-rays upon cancer. In some cases, the superficial epithelial growths, the tumor cells are destroyed, while in others there is little or no effect.

There are doubtless certain stages in the life history of every malignant tumor where the balance of forces is more or less equal, and at these periods the toxins are far more likely to be successful, than at other stages.

Again, the results vary necessarily greatly with the preparation of the toxins used. While the method of preparing the latter as described, is comparatively simple, many of the preparations that have been put upon the market have been so weak as to produce

scarcely any reaction, and, hence, proved to be of little value. The preparation that I have used the last twelve years in nearly all of my cases, was that made by Dr. B. H. Buxton, Professor of Experimental Pathology at Cornell Medical School, and whatever successes I have had with the toxins, are largely due to his bacteriological skill and hearty coöperation. The earlier successful cases were treated with the toxins made from the cultures of erysipelas obtained from a fatal case, and in the later cases the virulence of the cultures was kept very high by frequently passing the streptococcus through a series of animals.

Parke, Davis & Co., of Detroit, Mich., have made great efforts to improve their preparation and bring it up to the standard obtained by Dr. Buxton, and during the last two years they have come very near to it. For a long time the Parke, Davis & Co. preparation failed to show the deep red color, characteristic of the bacillus prodigiosus, and from long experience I have found the colorless toxins to be much less efficacious in producing an effect upon sarcoma. The reactions were likewise much less marked. Hence, I have come to regard the red color of the toxins as an important sign of their value. The reason for this has been lately shown by Dr. S. P. Beebe, who is making a series of experiments in connection with the Huntington Cancer Research Fund at the Loomis Laboratory, with various preparations of the toxins, and their effect upon animals in general, and upon sarcoma in dogs.

He has found that the bacillus prodigiosus grown in a deep flask, with little surface exposed to light and air, shows little or almost no color, whereas, when the cultures are grown in shallow vessels, with large areas exposed to light and air, the deep red color appears very soon. He has further demonstrated the fact that these red cultures develop much more powerful toxins.

Directions for the Preparation of the Mixed Toxins of the Streptococcus of Erysipelas and Bacillus Prodigiosus, According to the Formula of Dr. B. H. Buxton.

Broth. One pound of minced beef soaked over night in 1,000 c.c. of tap water. Then boiled for one hour, filtered through flannel. Add, peptone (Witte's), ten grams; NaCl, five grains. Test reaction to litmus and render alkaline by addition of sufficient quantity of ten per cent. NaOH. Boil for one hour. Sterilize by boiling half hour or three successive days; 25 c.c. of broth, in a small flask, is sown with streptococcus from culture in broth (a few c.c. of such culture being used). Allowed to grow in the incubator for three weeks. Then sown with bacillus prodigiosus (agar or broth culture), and allowed to grow at room temperature in the daylight (not direct sun) for ten days more. Poured in sterile bottles, heated to 60° in water bath for one hour; four to

five c.c of glycerin and a small lump of thymol added. Kept on ice until used.

Parke, Davis & Co.'s preparation is made in same way. The latter firm have recently made a new and stronger preparation, as follows:

FORMULA FOR MAKING SPECIAL ERYSIPELAS AND PRODIGIOSUS TOXINS (COLEY):

Enzyme peptone,	10	grammes.
Salt,	10	"
$NaPO_4$,	½	"

The reaction of the streptococcus media is such that the addition of 3 c.c. of normal NaOH per litre makes it neutral to phenolphthalein. The prodigiosus media requires 12 c.c. Whether this is any better than the preparation made in usual way, I have as yet been unable to determine.

As to the part the bacillus prodigiosus plays in causing the disappearance of sarcoma, its value rests entirely upon experimental or clinical data. Yet the fact that all of my own successes, as well as those of other surgeons, have been obtained by the combined toxins, not a single permanently successful case having been observed from the use of the erysipelas toxins alone, goes far toward establishing the importance of the bacillus prodigiosus.

In earlier years I experimented upon a large number of cases of inoperable sarcoma, first with the erysipelas toxins alone, and later with the erysipelas toxins combined with the prodigiosus, and I am quite convinced that the destructive effects of the erysipelas toxins were greatly increased by the prodigiosus toxins.

That this action is not merely a local action in the nature of an escharotic like carbolic acid, e. g., is proven by the fact that in numerous instances the tumor has disappeared from injections made remote from the locality of the tumor, showing it must have been due to a systemic rather than local influence. In most cases the best and quickest results are obtained by local injections showing a probability of both a local and a systemic action. This action I believe to be in the nature of a coagulation necrosis with a local leucocytosis. The tumor tissue at once becomes paler, loses its vascularity, undergoes fatty degeneration and subsequent absorption or breaking down. Which of these two results occurs is dependent upon the nature of the tumor and the general condition of the patient. As a rule the spindle-celled sarcoma, with fibrous tissues predominating, are more likely to disappear by slow absorption without breaking down or sloughing; while the more highly vascular growths, the round-celled type, are more likely to degenerate rapidly with the formation of sloughs.

As to the dosage, technique of administration and duration of

treatment, the only rules we have are those based upon experience. As a result of the personal use of the toxins in every variety of cases of inoperable sarcoma, extending now over a period of thirteen years, I would offer the following brief suggestions:

1. Always begin with a minimum dose, for the reason that individual susceptibility varies much and the vascularity of tumors varies more. The more highly vascular the tumor, the more severe the reaction.

2. For local injections the dose should be much smaller than for interstitial injections remote from the tumor. The initial dose for local injections (into the tumor) should be ¼ to ½ minim; for interstitial injections (remote from the tumor) one minim.

3. The dose should be gradually increased until a chill occurs (½ to 2 hours after injection), followed by a temperature of 101° to 103° or 104° F.

4. If there is much depression following the reaction and the patient's general condition is not very good, it is wiser to give the injections every other day, but if the patient can bear daily injections the chances of success are much greater.

5. In cases in which the tumor is situated in some region where injections are difficult or dangerous, e. g., within the abdomen or pelvis, it is better to give systemic injections, into the thighs, buttocks or abdominal wall.

6. If the tumor becomes soft and fluctuating, it is better to open the softened areas, establish drainage and treat with moist antiseptics.

7. A good tonic, preferably strychnine, quinine and iron, should be given during the treatment, and careful attention should be paid to keeping the bowels free.

8. *Duration of Treatment.* In successful cases a marked improvement is usually noted within one to four weeks. If no improvement has occurred at the end of four weeks of vigorous treatment, the chances are that none will occur, and little is to be hoped for more than a retardation of growth, and it may be wise to abandon the treatment or lessen the dose to the point of not making the patient uncomfortable by reason of chills. If, however, there is decided improvement, the injections should be continued until the tumor has totally or nearly disappeared. In some cases the treatment has been continued in small doses more than a year, and the patients are now well, many years after the cessation of treatment.

9. *Technique of Administration.* The toxins should be kept in a cool, dark place. The average duration of the treatment in the successful cases has been about two or three months, and the toxins seem to retain their strength for at least a year. Any good hypodermic syringe will answer, preferably one in which one minim

can be accurately estimated on the piston rod rather than on the barrel of the syringe. I sterilize the needle by an alcohol flame and pass boiling water through the syringe before and after using. In doses less than one minim the toxins can be diluted with boiled water; in doses larger than one minim no dilution is needed. The skin over the area into which the injection is to be made should be carefully cleansed with alcohol.

10. In cases after primary operation in which the toxins are given as a prophylactic against possible recurrence, smaller doses may be given, and it is not advisable to push them to the point of producing a chill; a slight rise of temperature, headache, and malaise are sufficient.

That the long-continued use of the toxins is not productive of harm, is proven by several cases in my own experience:

One patient with a twice recurrent, very rapidly growing carcinoma of the breast and axilla was given the toxins for two and one-half years. The tumor disappeared and the patient gained ten pounds in weight and remained well for over two years, when she developed general carcinosis with extensive abdominal involvement and died in a few months.

In another case, an eight times recurrent sarcoma (spindle-celled) of the chest wall (soft parts), the toxins were administered with occasional intervals of rest for nearly four years. The patient, a well-known physician, has had no treatment for over seven years and has been able to attend to his large practice the entire time.

Indication for the Use of the Toxins. While the curative action of the toxins varies greatly in different varieties of sarcoma, being most marked in spindle-celled, and least of all in melanotic sarcoma, I believe the toxins should be tried in practically every case of inoperable sarcoma, with the possible exception of cases with extensive generalization, and of melanotic sarcoma, with which I have had no permanent success; but there are cases of this type of sarcoma that have been cured by accidental erysipelas and cases which remained well four years or more under the mixed toxin treatment. I believe a trial worth while in such cases.

That no case of spindle- or round-celled sarcoma is too desperate to warrant a trial of the method, is shown by Cases XIX and XX.

At the time of my earlier paper, "The Treatment of Malignant Tumors by Repeated Inoculations of the Living Germ of Erysipelas" (AMERICAN JOURNAL OF THE MEDICAL SCIENCES, May, 1893), I had collected thirty-eight cases of malignant disease in which an attack of erysipelas had occurred, either by accident or design. The attack had occurred accidentally in twenty-three, and as a result of inoculation in fifteen. Seventeen cases were carcinoma, seventeen sarcoma, in four the type of growth was

doubtful. The results of these cases were, in brief, as follows: Of the seventeen cases of carcinoma three were permanently cured; in addition, one, a probable carcinoma, was well five years after the attack of erysipelas; the remaining thirteen showed more or less temporary improvement.

Of the seventeen cases of sarcoma seven, or forty-one per cent., were well and free from recurrence from one to seven years after the attack.

The type of tumor in these seven successful cases is worthy of note: One was a round-celled sarcoma of the neck; one, an osteo-sarcoma of the femur, recurrent; a third, a round-celled sarcoma, involving mouth, face and orbit, in a child ten years of age. The condition in this case was so desperate that death from exhaustion was daily expected. The tumor disappeared within a few days during an attack of erysipelas and the child was quite well, without any trace of a return a year after; a fourth case was a spindle-celled sarcoma of the neck; another, a melanotic sarcoma of the breast; another, still, was a multiple sarcoma of the face, and the seventh was a lympho-sarcoma of the neck.

In my own experience I have never seen either a case of melanotic sarcoma or lympho-sarcoma of the neck cured by operation.

The ten remaining cases showed more or less marked improvement. In some cases the tumor entirely disappeared and then recurred in the course of some months.

Since the time of publication of my paper just referred to, in 1893, I have endeavored to collect other cases in which erysipelas has occurred accidentally or otherwise in connection with malignant tumors. Although these cases are few in number, they confirm what has already been said. These new cases are as follows:

Case I.—*Cancer of the breast, covering an area of about sixty square inches. Reported by F. C. Boomer, of Chicago. (Personal communication.)* Entered hospital to die; violent erysipelas infection. Tumor disappeared in the course of six weeks. No recurrence in nine years.

Case II.—*Ibid.* Sarcoma of the neck, the size of an orange; erysipelas inoculation; entire disappearance of tumor; patient alive and free from recurrence eight years later.

Case III.—*Ibid.* Cancer of the face that developed in the scar of an old burn; eighteen years' duration; erosion of lower eyelid and ala of nose; entire disappearance immediately following an attack of erysipelas, after the patient had been pronounced hopeless; recurred locally several years later; was then treated by the daily injections of the mixed toxins; a typical epitheliomatous ulcer, the size of a silver dollar, healed after one month's treatment; the treatment was continued for one month

longer; patient discharged cured. Patient moved to Dakota, from where he wrote six months later that there was a local recurrence.

CASE IV.—*Large epithelioma of face, cheek, lip and nose; Dr. Copeland, Round Hill, N. J.* Patient aged eighty-five years. Entire disappearance under an accidental attack of erysipelas. Patient died of other trouble two years later, without recurrence.

CASE V.—*Dr. C. C. Brockner, Ottumwa, Ia., 1890.* Case a female, aged seventy-one years; typical epithelioma of the face of one to two years' duration, the size of a silver dime; ulcerated one year. Severe attack of erysipelas in the spring of 1897, with temperature of 104° to 105°. Ulcer entirely healed in two months. Patient well six months later.

CASE VI.—*Dr. H. M. Neale, Upper Lehigh, Pa. Epithelioma of nose.* Size of a silver quarter; eight years' duration. Severe attack of facial erysipelas, extending over entire head. Epithelioma disappeared during and shortly after attack of erysipelas had subsided, and there has not been any recurrence up to present time, several years.

Following are a few cases apparently showing the value of erysipelas infection as a prophylactic agent:

CASE I.—*Extensive cancer of both breasts. Dr. Boomer.* Speedy recurrence anticipated; severe erysipelas infection during course of wound healing. Patient alive and well for seven years.

CASE II.—*Epithelioma of the ear, involving parotid back of glands. Dr. Rudolph Matas.* Incision, but not regarded as complete, and almost certain recurrence expected. Severe attack of erysipelas developed during wound healing. Patient alive and well four years later.

CASE III.—*Dr. H. M. Neale, Upper Lehigh, Pa. (Personal communication.) Lympho-sarcoma of neck. (Microscopical examination.)* Male, aged twenty-eight years. 1897. Tumor size of egg. Supra clavicular region of neck; three months' duration. Extended deeply behind sterno mastoid muscle; removal probably not complete. Extensive suppuration followed operation, with discharge of "bloody pus" for a month. Finally healed, and patient was well when last heard from eight years later. (In this case while there was no attack of erysipelas there was probably a streptococcus infection. Toxins obtained from the streptococcus pyogenes have nearly if not quite the same effect upon sarcoma as those obtained from the streptococcus erysipelatis.)

CASE IV.—*Dr. Neale. Spindle-celled sarcoma of breast and pectoral muscle.* Female, aged thirty-six years. 1899. Tumor of left breast size of a baseball. Operation, removal of tumor, breast, axillary glands and part of pectoral muscle. Two days later severe attack of erysipelas, with considerable purulent discharge. Recovery; in perfect health at present, seven years later. Micro-

scopic examination of specimen made at laboratory of Jefferson Medical College showed it to be spindle-celled sarcoma.

Metastases. When the sarcoma has become generalized, as shown by the presence of distinct metastases, the prognosis is naturally much more grave. Formerly, I was inclined to advise against the use of the toxins in such cases. Yet there have been a number of successful results in just such conditions, e. g., the case of Battle of London, the case of Dr. Winberg, and, especially, two of my own cases. In one, the case reported in my earlier papers, of sarcoma of the back with extensive metastases in the groin, the patient recovered and remained well for 3¼ years, and afterward died of internal metastases. In the other case, a round-celled sarcoma of the femur, there was a very large metastatic tumor in the pectoral region, and one, the size of a child's head, in the lumbar and iliac region, which disappeared, and the patient is alive and well more than three years afterward. The case of sarcoma of the spine reported in full (*vide* Case XIX), with extensive emaciation and total paralysis of the lower extremities, bladder and rectum, with perfect recovery, and the patient in good health four years later, proves that no case is so desperate as not to be worthy of a trial of the treatment.

I have called attention in other papers to the possible danger of producing metastases from the use of the X-rays in malignant tumors, especially sarcoma, and I have cited cases in my own experience in which very extensive metastases seemed almost certainly produced by the too rapid breaking down of sarcoma of lymphatic glands under the X-rays and the infected cells entering the circulation and being carried to remote parts of the body. The most conclusive case of this kind was a very large lympho-sarcoma of the neck. The tumor disappeared very rapidly under the influence of the X-rays, but soon recurred and the patient finally died with the most extensive generalization of the disease that I have ever observed. Not only were there internal metastases, but hundreds of subcutaneous tumors, varying in size from a pea to an English walnut, in every portion of the body from head to foot. The fact that in lympho-sarcoma general metastasis is extremely rare, makes the case all the more significant. With the mixed toxins of erysipelas and bacillus prodigiosus we have even more rapid degeneration and absorption of sarcoma than with the X-ray, and in a much larger number of cases, and at once the question arises, "Why does metastasis not occur in the same way?" I can only say I have never seen any case which seemed to indicate such a result. The explanation may be offered that in the case of the toxins certain changes in the blood serum have been brought about by the toxins which make it destructive to the tumor cells, which have gained access to the circulation, making it impossible to set up new foci of disease where they happen to lodge, while in the

case of the X-ray the action is merely local, and the infected cells when transported to other localities of the body, find favorable conditions for growth. But, whatever the explanation, the facts are as I have described, at least in my own observation.

The Value of the Toxins as a Prophylactic After Primary Operation for Sarcoma or Carcinoma.

Theoretically, it would seem only logical that an agent that has the power of destroying a large inoperable tumor, would be more likely to destroy the few infected cells that remain behind after primary operation and give rise to future recurrence. Yet, this is a question, the final settlement of which, will require many more cases than I have been able to gather, and observations for a much longer duration of time. In view of the fairly well demonstrated fact that an attack of erysipelas occurring during wound healing after operation for primary tumor, lessens the chances of recurrence, and, assuming that the curative value of the erysipelas lies chiefly, if not wholly, in the toxins, the theoretical reasons for using the toxins after primary operation seem well grounded. Up to the present time I have not felt that the number of observations were sufficient to warrant me in advising such treatment as a routine measure, but I am gradually becoming convinced of the wisdom of so doing. I have used the toxins as a prophylactic after operation in the following cases:

Case I.—*Mrs. C., Mixed-celled sarcoma of the finger.* Removed under cocaine, without amputation, under the belief that the growth was benign. Diagnosis of sarcoma confirmed by Prof. W. H. Welch. Amputation considered, but toxins first tried as a prophylactic. Patient alive and well seven years later.

Case II.—*Sarcoma of the deltoid region.* Toxins given shortly after operation, when there was a suspicion of a recurrence. Suspicious thickening disappeared; patient well three years.

Case III.—*Spindle-celled sarcoma of the hand and axilla.* Recurrent four times, always within a few months after each operation. Patient well when last heard from, a year later.

Case IV.—*Round-celled sarcoma of the gracilis muscle of thigh.* Toxins immediately after last two operations, in large doses, in addition to X-ray; apparently no effect whatever in preventing a recurrence.

Case V.—*Sarcoma of the thigh.* Recurrent in stump after amputation; removed as well as possible by operation; toxins given later and continued for several weeks, did not prevent recurrence.

Case VI.—*Sarcoma of the thigh muscles.* Considered inoperable, except by amputation. Toxins for three months; at first the tumor nearly disappeared; then gradually became beyond control. Hip joint amputation with every expectation of quick re-

currence as the disease extended nearly up to the flap. Toxins given; no recurrence; patient well six years afterward.

CASE VII.—*Double carcinoma of the breast.* Considered quite hopeless by Dr. Maurice H. Richardson, of Boston, in 1895. Recurrent mass on one side, four inches square, removed, and toxins given immediately afterward; continued in small doses, with intervals of rest, for several years. Patient from time to time had small subcutaneous nodules appear of very low type of malignancy. She lived for nearly ten years, then died of abdominal metastases.

CASE VIII.—*Round-celled osteo-sarcoma of Humerus.* X. X., patient of Dr. J. B. Blake, of Boston, was operated upon, by him, in 1899, the operation consisting in removal of the head of the humerus, tip of the coracoid and part of the glenoid cavity. Immediately after the wound had healed the mixed toxins were begun and continued for a number of months.

Examination made by Dr. Blake on December 11, 1903, four years later, showed the patient to have gained ten pounds in weight, and to be performing her regular work as housemaid.

CASE IX.—*Round-celled sarcoma of the testis.* J. G., aged fifty-two years. Operation for round-celled sarcoma of the testis performed in 1901. Recurrence within one year. A second operation was done, removing the other testis, after which the toxins were given as a prophylactic. The patient is doing well at present, nearly two years later.

CASE X.—*Carcinoma of the breast, three times recurrent.* Mrs. B., aged forty years. The first operation was performed on January 19, 1894; the second by myself, in June, 1895. It was impossible to remove all of the infected glands from the axilla. One gland, the size of a hickory nut, high up in the axilla, and completely surrounding the axillary vein, had to be left behind. Local recurrence took place in the cicatrix before the wound had entirely healed, and progressed rapidly. The arm soon became swollen and the pectoral muscles showed marked infiltration. The patient was then put upon the mixed toxins, the injections being given two to three times a week. The treatment was continued with intervals of rest, for nearly two years. At the end of six months the mass in the axilla could no longer be felt. An area of local recurrence in the cicatrix was excised. The right arm which had been two inches larger than the left, was reduced so that its circumference was only one-half inch greater than that of the other. The patient remained well until the summer of 1897, two years, when the toxins were left off for a period of five weeks. During this time the local tumor increased rapidly in size and evidence of extensive metastases in the liver and abdomen appeared. The patient died in December, 1897, two

and one-half years later. Microscopic examination proved the tumor to be a typical carcinoma.

Case XI.—Miss S., aged thirty-three years. Removal of right breast and axillary glands for carcinoma in May, 1902. The patient was put upon the X-ray treatment immediately afterward as a prophylactic. Six months later, while still under X-ray treatment, small recurrent masses were noticed in the skin along the line of the old cicatrix. These were excised on two occasions and the X-ray treatment resumed. Later there appeared an extensive infiltration in the region of the scar and pectoral region, with a marked œdema of the arm. The X-ray treatment was then abandoned, and, in June, 1904, the patient was put upon small doses of the mixed toxins (1 to 2 minims), given in the pectoral region. The treatment has been continued, with occasional intervals, up to the present time. The mass in the pectoral region has entirely disappeared, and the arm, which at one time was two inches larger than the other, is now only one-fourth inch larger. On the other hand, her general health is not as good at present as it was a year ago. She has lost some weight, and there is a possibility of internal metastases having taken place, although no palpable evidence exists at present in the last two cases.

In several of these cases the operations were incomplete and the tumor tissue was not all removed.

These cases of carcinoma show that the toxins do have a marked inhibitory action, even in carcinoma, and although this is rarely curative, I believe it sufficient to justify the routine use of the toxins after all primary operations for carcinoma, as well as for sarcoma.

Final Results of Personal Cases.

Of thirty-six cases which may be fairly classed as successful, in that the tumor disappeared under the injections with the mixed toxins, the type of the neoplasm was as follows:

13.....Round-celled.
16.....Spindle-celled.
2.....Mixed-celled.
1.....Epithelioma.
1.....Chondro sarcoma.
3.....No microscopical examination made, but the clinical appearance, together with the history of recurrence, left practically no room for doubt as to the diagnosis.

The results in these cases, thus far, have been as follows:

5.....Well less than a year.
4.....Well from 1 to 2 years.
3.....Well from 2 to 3 years.
5.....Well from 3 to 5 years.
21.....Well from 5 to 13 years.
(Ten cases well over ten years.)

In five cases a recurrence took place and finally proved fatal. In one of these recurrent cases the patient had remained well eight years; in one, 3¼ years; in one, 2½ years; in one, seven months; in one, six months.

These five cases of recurrence are, perhaps, the most important of all, inasmuch as they furnish absolute proof of the correctness of the diagnosis, and refute the early objections brought against

the method, that the successful cases were probably examples of errors in the diagnosis.

That in twenty-six (personal) cases the patients were alive and well from three to thirteen years after treatment, would mean a good deal if we were dealing merely with primary operable sarcoma, but when we consider that all of these cases were beyond operation, and were absolutely hopeless, as regards treatment of any hitherto known method, it means far more. Look for a moment at the results of operations for cancer of the stomach which are receiving such a large share of attention at present, and which are advocated more and more strongly each year. In one of the most recent and valuable books ("Abdominal Operations," by Moynihan, 1905), the results at one of the leading surgical clinics of Europe, and one with, perhaps, the largest experience in stomach surgery, show that of 209 cases of cancer of the stomach operated upon, only two cases were alive and well beyond three years.

The value of any method in the treatment of malignant tumors depends not upon the number of cases in which the tumors have disappeared, but upon the number of cases in which the patients are alive a sufficient number of years to warrant us in calling them cured, in other words, upon the test of time. I have made great efforts to trace not only my own cases, but also those successfully treated by other surgeons, with the following results:

Final Results of Cases Treated by Other Surgeons.

From published reports and personal communications from other surgeons who have tried the mixed toxins in inoperable sarcoma, I have tabulated sixty cases of complete or partial success.

Of these cases—

22 were sarcoma of the round-celled variety.
14 spindle-celled.
3 mixed-celled.
3 endothelioma.
2 epithelioma.
16 in which no microscopical examination was made.

or it was not recorded, but in all of these cases the clinical diagnosis was confirmed by a number of surgeons, and the patients were considered hopeless from an operative standpoint. The results in these cases were as follows: Twenty-seven patients were alive and well from three to twelve years.

12 remained well less than a year.
In 6 the tumor disappeared and the patient was alive and well from 1 to 2 years.
" 9 the tumor disappeared and the patient was alive and well from 2 to 3 years.
" 12 the tumor disappeared and the patient was alive and well from 3 to 5 years.
" 10 the tumor disappeared and the patient was alive and well from 5 to 12 years.
" 5 cases recurred within periods of from six months to two years.
2 died during treatment.

One, a case of A. Marmaduke Shield *(Brit. Med. Jour.,* Jan. 23, 1897), a recurrent, inoperable round-celled sarcoma of the breast. The tumor disappeared by breaking down and sloughing, but the patient died of pyæmia, staphylococcus infection while still under treatment. The second, was a case of M. L. Harris, of Chicago (personal communication), a recurrent, inoperable sarcoma of the ovary involving the rectum. The toxins were used for four weeks, the injections being made into the arm. Very marked improvement was noted, the tumor decreased greatly in size, resulting in a final sloughing of the entire tumor. The patient died a month later of septic absorption.

This latter case is of great value as showing the systemic influence of the toxins.

Nine cases were alive and well, without recurrence, from five to eleven years.

In nine of my successful cases, the sarcoma originated in the bone; in twenty-two, in the soft parts (external); five were intra-abdominal growths. In seven cases the injections were made remote from the tumor, usually into the tissues of the thighs or abdominal wall, proving that the tumors in these cases disappeared entirely as a result of the systemic action of the toxins.

Of the successful cases in the hands of other surgeons, twenty occurred in the bones; no less than nineteen were intra-abdominal growths; only fourteen occurred in the soft parts, other than the abdomen. In twenty cases the injections were made remote from the tumor into the tissues of the thigh or abdominal wall. In the remaining cases the injections were made locally into the tumor. The bone sarcomas were distributed as follows:

Three of the tibia, one of the fibula, four of the superior maxilla, three of the femur, one of the spine, two of the ribs, two of the radius, one of the humerus, one of the orbit, one of the lower jaw, one of the sternum.

The Use of the Toxins Before Resorting to Amputation in Cases of Sarcoma of the Extremities.

This is a very important question and one upon which I have avoided expressing a positive opinion until a sufficient number of facts have been collected to justify such an opinion. Up to the present time I have been able to collect twelve cases of sarcoma of the extremities, three personal cases, and nine reported by other observers, in which the use of the mixed toxins has rendered amputation unnecessary and the limb has been saved.

In eight of these cases the sarcoma was of the round-celled variety; in two, of the spindle-celled, and in two no microscopical examination was made, but amputation had been strongly advised in both instances, by a prominent surgeon.

The period of observation of these cases is most important:

Eight were alive and well and free from recurrence from three to six years.
Two were well at the time of the last observation, at the end of one year.
Two other cases were observed less than six months.

In all these cases, with but one exception, the tumor was of bony origin:

5 of the tibia.
1 of the fibula.
2 of the femur.
1 of the forearm.
1 of the humerus.
1 of the thigh, involving the periosteum.
1 of the calf of the leg.

In every one of these cases amputation had been seriously considered, but it seemed justifiable to give the toxins a trial before resorting to operation.

These cases seem to me sufficient in number, and the period of observation sufficiently long, to justify us in advising preliminary toxin treatment in nearly all cases of sarcoma of the extremities before resorting to amputation.

REVIEW OF MORE IMPORTANT PERSONAL CASES, WITH SUBSEQUENT HISTORY.

CASE I.—*Recurrent inoperable spindle-celled sarcoma of neck and tonsil,* treated with injections of living cultures of erysipelas for four months, with the result that the tumors nearly disappeared and the patient recovered his usual health. He remained well for eight years and finally died of a local recurrence.

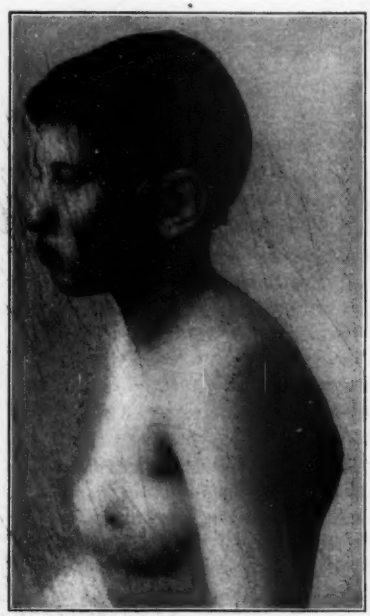
CASE II.—*Recurrent sarcoma of back and groin, mixed-celled, round, oval and spindle.* Male, aged forty years. First treated in April, 1892, with repeated injections of living bouillon cultures of erysipelas. Entire disappearance; rapid recurrence two months later, final disappearance under the mixed toxins. The patient remained well three and one-fourth years, and in September, 1896, had an intra-abdominal recurrence in the retroperitoneal region. The tumor increased rapidly in size. In November, 1896, the patient became markedly jaundiced, but at the end of six weeks the jaundice disappeared and did not return. He gradually failed and died in April, 1897. Autopsy showed a large, hard tumor starting behind the posterior parietal peritoneum, pressing the viscera forward against the abdominal wall. The pathologic report of the original tumor made by Dr. Farquhar Ferguson, of the New York Hospital was given in full in a former paper. (AMERICAN JOURNAL OF THE MEDICAL SCIENCES, Feb., 1893.)

For a full report of these two cases, see beginning of this paper.

CASE III.—*Inoperable spindle-celled sarcoma of the abdominal wall and pelvis.* Entire disappearance of the tumor under four months' treatment with the mixed filtered toxins; well at present, five years later. Patient male, aged sixteen years, admitted to the New York Cancer Hospital in January, 1893, having been referred to me by Dr. L. Bolton Bangs as a totally inoperable sarcoma, the diagnosis having been confirmed by microscopic exam-

ination by Dr. H. T. Brooks, pathologist at the Post-Graduate Hospital. The entire tumor, 7x5 inches, completely disappeared. The patient has been in perfect health ever since, and I examined him December 20, 1905, and found no trace of a recurrence, thirteen years after treatment. (About six years ago he developed primary syphilis.)

FIG. 2



Spindle-celled sarcoma. Chest wall. Disappeared under mixed toxins. Case V.

FIG. 3

Ibid.

CASE IV.—*Inoperable sarcoma of the abdominal wall.* Entire disappearance under two and one-half months' treatment with the mixed toxins (filtered and unfiltered). The patient, a woman, aged twenty-eight years, had had an exploratory laparotomy performed in August, 1893, at the Massachusetts General Hospital, by Dr. Maurice H. Richardson. A tumor was found involving such a large portion of the abdominal wall that removal was impossible; a portion was excised and pronounced spindle-celled sarcoma by the hospital pathologist, Dr. W. F. Whitney. She was

referred to me in October, 1893, by Dr. Richardson. The patient has remained in perfect health, and there had been no trace of recurrence on December 10, 1905, twelve years.

CASE V.—*Spindle-celled sarcoma of the scapula involving large part of left half of the thoracic wall.* Entire disappearance of the tumor under three months' treatment with the mixed unfiltered toxins. This is one of the most striking cases of success with the toxins. The patient, a girl, aged sixteen years, was admitted

FIG. 4

Same 1½ years later. Patient well ten years later. Case V.

FIG. 5

Ibid.

to the New York Cancer Hospital, June 20, 1894. The tumor had started in the left scapular region, four months before, and had grown very rapidly until the time of admission; the tumor measured thirteen inches vertically behind and extended around beneath the axilla and to the sternum in front. The growth was fixed to the scapula and to the ribs, and probably originated in the soft parts over the scapula; it was about two inches in thickness in its most protuberant part, the skin over it being normal and perfectly movable. The left arm was bound down by the new

growth so that it could scarcely be raised to a horizontal position. The mixed, unfiltered toxins were injected locally into the scapular portion of the tumor and continued with intervals of one to two days for nearly four months. Immediate and very striking improvement followed; at the end of three weeks the arm could be raised to a vertical position. After three months' treatment the tumor had entirely disappeared by absorption only, without breaking down. There was no evidence of inflammatory, tuberculous or specific disease. The diagnosis of spindle-celled sarcoma was moreover confirmed by careful microscopic examination by Dr. H. T. Brooks, pathologist to the Post-Graduate Hospital. The patient was in good health in 1904, when last heard from, ten years after treatment.

Case VI.—*Intra-abdominal round-celled sarcoma.*—E. J., female, aged twenty-three years; born in Switzerland; in the United States six years. In 1894 she began to have pain in the right hypochondriac region, soon becoming so severe as to confine her to bed. August 16, 1894, operation by Dr. Willy Meyer, at the German Hospital; exploratory laparotomy showed a tumor the size of an orange springing from the mesentery of the small intestine, but attached to the omentum and gall bladder. It was found impossible to remove the growth, but a portion was excised for microscopical examination and the abdomen closed. It proved to be a small round-celled sarcoma. As soon as she recovered from the operation, she was referred to me by Dr. Meyer for the toxin treatment. At this time there was a sinus remaining at the site of the incision, and on palpation a hard mass, about four inches in diameter, could be felt deep in the abdomen. The mixed toxins were begun immediately, injections being made alternately in the abdominal wall and buttocks. The treatment was kept up with occasional intervals until February, or about five months, at the end of which time there remained only an indistinct resistance at the site of the tumor; the patient's general health was perfect. On January 25, 1896, an attempt was made to close the sinus which had been closed for some time, but re-opened. At this time she was examined by Dr. Bull and no tumor could be discovered. When cutting down as far as the peritoneum, the probe entered a sac containing two to three ounces of muco-purulent material and several gall-stones, one of which was impacted in the cystic duct. No evidence of a tumor could be detected in the abdominal cavity. The sarcomatous mass, which was originally adherent to the gall-bladder when it broke down under the toxins, probably caused an opening in the gall-bladder, which soon became connected with the sinus. Dr. Meyer, in describing the operation, states that clinically the tumor had every appearance of a malignant growth, probably sarcoma. To remove the growth radically seemed impossible, as such an operation would have had to consist in resection

of a portion of the large, as well as small intestine, and a portion of the liver, as well as the omentum. A wedge-shaped section was removed and pronounced round-celled sarcoma by Dr. F. Schwyzer, pathologist to the German Hospital. The patient has remained in perfect health up to present time, eleven years.

CASE VII.—*Inoperable recurrent angiosarcoma of the breast, treated with erysipelas and prodigiosus serum, later by the mixed toxins.*—The patient, female, aged fifty-nine years, had a three-times recurrent sarcoma of the left breast, of such size that operation was entirely out of question. She was referred to me by Dr. George F. Shrady, of New York, as an inoperable case. She was

FIG. 6

Recurrent angio-sarcoma. Round-celled of breast. (Exam. Prof. T. M. Prudden.) Disappearance under toxins. Patient well eight years later. No. I.

admitted to the New York Cancer Hospital, January 20, 1895, and placed in the incurable ward. Physical examination showed a tumor occupying the region of the left breast extending from the anterior axillary line to the sternum, and from just below the clavicle nearly to the free border of the ribs; it was more or less fixed to the chest wall, and markedly protuberant. The patient's general condition was so bad that no attempt was made at first to give her the toxins; she was treated with small doses of erysipelas and prodigiosus serum, prepared by Dr. Buxton. Later the mixed toxins were used. The tumor slowly shrunk in size and the patient's general condition improved; by September, 1895, the tumor had become so much reduced in size and was so loosely attached that

it was easily excised under ether. The diagnosis was confirmed by microscopic examination by Prof. T. M. Prudden, of Columbia University, who pronounced it round-celled angiosarcoma. This patient remained well until 1903, eight years, when she fell down stairs and suffered injuries which proved fatal. She was examined at this time by my associate, Dr. W. A. Downes, who found no trace of recurrence.

CASE VIII.—*Inoperable spindle-celled sarcoma of the pectoral region and breast; disappearance under seventy-eight injections of the mixed toxins.*—E. F., aged forty-two years. Father's mother died of cancer of the breast. Previous health good. She first

FIG 7

Angio-sarcoma round-celled of breast. After several weeks of toxin treatment. No. II.

noticed a lump in the left pectoral and axillary region in October, 1895. This grew rapidly until it reached the size of an orange; it was firmly adherent to the deep parts and extended well into the axilla. On December 15, 1895, the patient was admitted to the Hartford Hospital, and after consultation between Drs. Storrs and Knight, and others, her condition was pronounced quite inoperable. A portion of the tumor was removed under cocaine. Microscopic examination showed it to be spindle-celled sarcoma. I obtained sections of this tumor from Dr. Storrs, and the diagnosis was confirmed by Dr. E. K. Dunham and Dr. B. H. Buxton, of New York, and, finally, by Prof. W. H. Welch, of Johns Hopkins

Medical School. The patient's general health had become poor, and she had lost twenty-four pounds in weight. The treatment with the mixed toxins was immediately begun by Drs. R. H. Griswold and Storrs under my direction. Almost immediately after the beginning of the treatment, the tumor began to decrease in size, and in little more than one month's time, she had regained her normal weight of 154 pounds. After she had had seventy-eight injections, the tumor entirely disappeared and she received no further treatment. I presented the patient before the New York Surgical Society in November, 1896. She has remained in perfect health up to the present time, more than ten years afterward.

FIG. 8

Angio-sarcoma of breast. Round-celled. After treatment. No. III.

CASE IX.—*Mixed-celled sarcoma of the parotid, three times recurrent, treated with injections of the mixed toxins for six months; patient perfectly well ten years later.*—Mrs. B., aged twenty-five years; previously operated upon three times by Dr. William T. Bull for mixed-celled sarcoma of the parotid. She was referred to me by Dr. Bull in 1895 for the toxin treatment, as there was no hope of benefit by further operation. At this time the tumor was about the size of a small egg, infiltrating the entire parotid gland on

the right side; cervical glands not enlarged. The mixed toxins were given in small doses two to three times a week, with occasional intervals for four months. The tumor slowly decreased in size until there was a very small, freely movable nodule left, which was excised under examination, showing no longer any traces of sarcoma. The patient has remained in perfect health up to the present time, January, 1906, ten years later.

CASE X.—*Spindle-celled sarcoma of iliac fossa, probably starting in the ilium.*—Mrs. D., aged forty years, with a good family history, in the early part of 1895 began to have sharp, stinging pains in the right iliac region. In May, 1895, she discovered a tumor in this region. This steadily increased in size, and on October 19, 1895, Dr. Johnston, of Boston, performed an exploratory laparotomy. He states: "A tumor was found in the right iliac fossa about the size of a cocoanut, attached to the ilium, as well as to the abdominal wall, and totally inoperable. Its exact point of origin could not be made out, but from the exploration and subsequent examination, I am convinced that it started from the inner portion of the crest of the ilium." A part of the tumor was excised and examined by Dr. William F. Whitney, pathologist to the Massachusetts General Hospital, who pronounced it "spindle-celled sarcoma." In November, 1895, the patient was treated with injections of the mixed unfiltered toxins (Buxton) by Dr. Farrar Cobb, of Boston. In a letter Dr. Cobb states: "At the end of six weeks' treatment the growth has entirely disappeared."

On May 17, 1896, the patient came to me with a recurrence and entered the New York Cancer Hospital. Examination at that date showed a hard mass on the right side, extending from the crest of the ilium nearly to the level of the umbilicus and as far to the left as the median line. The tumor was apparently located in the ilium and abdominal wall. Her general health was excellent. The toxins were at once begun and continued with intervals of rest for three months. The outline of the tumor gradually receded toward the crest of the ilium, and when she was discharged from the hospital the tumor was not more than one-fifth its original size when I commenced the treatment. She left with the understanding that she was to return in the fall and resume the injections. She was readmitted to the hospital in November.

Examination showed the tumor to have increased considerably in size during the interval of rest, but on beginning the treatment the tumor at once began to shrink. Whenever the injections were made the patient noticed a peculiar burning feeling in the tumor, and this was true whether the injections were made into the abdominal wall or into the thigh. The abdominal wall was so thick with fat that few of the injections were made into the tumor itself. This patient was one of the very few I have seen in whom the toxins always produced very severe irritation in the skin.

After each puncture a hard, indurated and very painful area the size of a half dollar would appear, and this would not pass away entirely for several days. When she left the hospital, June, 1897, the tumor had remarkedly decreased in size, and entirely disappeared a few months later. I have examined her a number of times since, the last time in January, 1906, ten years after treatment. She is in perfect health and has been the entire time, and no trace of a tumor can be felt.

FIG. 9

FIG. 10

FIG. No. 7.—Inoperable epithelioma of floor of mouth, lower jaw, and chin. Disappearance with toxins. Well six years. No. I.
FIG. No. 8.—Epithelioma of floor of mouth, lower jaw, and chin. No. II.

CASE XI.—*Inoperable epithelioma of the chin, lower jaw and floor of mouth.* The mixed toxins were used for four months. Entire disappearance. The patient well without recurrence six years afterward. This case has already been fully reported in a former paper. The patient was referred to me by Dr. George R. Fowler, of Brooklyn, who regarded it as entirely inoperable. Microscopic examination was made by Dr. William Belcher, pathologist of the Seney Hospital, of Brooklyn. It is but fair to say that the microscopic examination was made from frozen sections, and I wish to give due weight to whatever doubt there may be attached to the diagnosis. The fact remains that the operation

proposed for the condition, by an eminent surgeon, was entire removal of the lower jaw, floor of mouth and portion of the tongue. In view of the dangers attached to this operation, and the chances of a speedy recurrence, the surgeon advised against it. The tumor entirely disappeared under four months' treatment with the toxins, and the patient continued well six years afterward.

CASE XII.—*Spindle-celled sarcoma of the foot, metatarsal bone, recurrent in leg and thigh. Final disappearance; patient well nine years.*—F. K., female, aged sixteen years; had a fall in 1888, injuring right foot. Shortly after two lumps appeared in the foot in the region of the injury and grew steadily until 1889. The patient was operated upon by Dr. William T. Bull, at the New York Hospital, the third and fourth metatarsal bones being removed. Three years later she received another injury to the foot, followed quickly by recurrence. A second operation—Syme's amputation—was then performed by Dr. Bull. In 1893 she fell down stairs, injuring the stump; shortly afterwards a lump appeared at the outer aspect of the stump, which slowly increased in size. Very soon a tumor appeared in the popliteal space which grew with great rapidity until December, 1893, when it had reached the size of a child's head, when it was removed by Dr. Bull. The tumor in the stump was treated by Dr. Bull and myself with the mixed toxins of erysipelas in January, 1894, with the result of entire disappearance. One and a half years later there was a recurrence in the stump, as well as in the popliteal region, and in 1896 I did a high amputation just below the trochanter, which was again followed by recurrence in the gluteal region. This was partially removed by operation and the toxin treatment was resumed and continued with intervals for three years. The tumor disappeared and the patient has remained entirely well up to the present time, December, 1905, nine years after the final disappearance of the disease.

CASE XIII.—*Sarcoma of the sacrum. Patient in perfect health at present, eleven years later.* H. B. H., male, aged thirty-eight years, born in Ireland, lived in the United States for twenty years. No history of injury. In February, 1895, the patient began to lose flesh and strength; soon after had pain in the lower part of the spine over the sacrum, the pain extending down the legs, more marked on the right side; consulted Dr. W. C. Deming, of Westchester, in April, 1895. At this time he had slight lameness of the right leg, which was followed shortly afterward by lameness of the left leg. All symptoms progressively increased, the pain becoming very acute, so much so that the patient wished to die. On May 2d he was sent to St. Luke's Hospital, service of Dr. Francis P. Kinnicutt. His normal weight of 175 pounds had fallen to 134 pounds, and he could walk with the greatest difficulty only. Careful examination of the rectum

at this time showed a large, hard tumor, attached to the anterior portion of the sacrum, the lower border of which could be reached by the index finger. The tumor was of firm consistence and very firmly fixed; its upper outline could not be determined. The patient was markedly emaciated and his general appearance characteristic of malignant disease. The diagnosis of Dr. Kinnicutt as well as that of the other attending physicians and surgeons who saw him in consultation, was inoperable sarcoma of the sacrum and pelvis.

I saw the patient in consultation on May 10, 1895, and advised a trial with the toxins for two to three weeks, to be then discontinued if no improvement was noticed. The injections were made directly into the buttocks and repeated daily. At the end of one week the pain had almost entirely subsided and the lameness was much improved. The improvement continued rapid and constant; at the end of six weeks he returned to his home, where the injections were continued for some time, two to three injections a week being given by Dr. Deming evenings, so as not to interfere with his regular occupation, which he had resumed. At the end of seven weeks the patient had gained twenty-eight pounds in weight and stated that he felt as well as ever. Two years later his weight was 176 pounds. He is in perfect health at present, nearly eleven years later.

Case XIV.—*Round-celled sarcoma of the parotid. Patient free from recurrence at the present time, four and one-half years after disappearance of the tumor, under eight months' treatment with the mixed toxins.*—Mr. M. E. S., aged fifty-five years, born in the United States; family history good; previous history always well; no trauma. He noticed a lump in the right parotid region in the fall of 1899. The tumor increased rapidly in size; when it was about as large as a hen's egg, it was operated upon by Dr. William T. Bull on April 5, 1900. Pathological examination of the specimen by Dr. M. P. Denton showed it to be a small round-celled sarcoma. This opinion was verified by Dr. William H. Welch, of the Johns Hopkins Hospital. Shortly after this a local recurrence was noticed which increased steadily in size until October, 1900, when it was decided by Dr. Bull that further operation would be unadvisable, and the patient was referred to me for the mixed toxin treatment. The injections were begun on October 5, 1900, and continued daily for one month, doses ranging from one to two minims, causing temperature reactions ranging from 99° to 102°. At the end of one month the improvement was so slight that the propriety of continuing the treatment seemed questionable. However, it was decided to give the patient a further trial and the injections were kept up from four to five times a week during the entire winter. At the end of three months there was a marked improvement. On April 1, 1901, the

tumor was about one-fourth of its original size. The treatment was continued until June with gradually diminishing frequency. By this time the tumor had entirely disappeared. The patient has remained in good health, without recurrence up to the present time, February 10, 1906. The patient was in perfect health during the entire time of treatment, and was at no time confined to his bed.

CASE XV.—*Spindle-celled sarcoma of the abdominal wall and pelvis. Entire disappearance under thirty injections with the mixed toxins. Patient well one and one-half years later, when she returned to her home in Europe.*—M. S., aged eighteen years; admitted to the New York Cancer Hospital, December 29, 1896. Family history, negative. The patient had a tumor in the lower portion of the abdomen of some months' duration, associated with slight pain. The growth could be felt both through the abdominal wall and by vaginal examination. Exploratory laparotomy was performed on January 2, 1897, by Dr. Joseph Brettauer, and Dr. George W. Jarman. On opening the abdomen, a large mass was found both intra- and extra-peritoneally; it had no connection with any of the abdominal organs and was located chiefly in the abdominal wall, but its point of origin could not be exactly determined. It was decided to be inoperable, and the wound was closed, a portion of the tumor having been removed for microscopical examination. The examination was made by Dr. E. K. Dunham, Professor of Pathology at Bellevue Medical School, and Dr. B. H. Buxton, both of whom reported the tumor to be a spindle-celled sarcoma. On January 17, 1897, the patient was transferred to my service for the toxin treatment. Examination at this time showed a large mass just above the symphysis pubis extending nearly to the umbilicus, and from 1 inch to the left to 2 inches to the right of the median line, smooth in outline, firm in consistence, the skin over it being very movable. The injections with the mixed toxins were begun on January 19th; the first injection consisted of 3 minims of the filtered toxins made from cultures which had been passed through fifty-six rabbits, and of a high degree of virulence. A temperature reaction of 99.8° followed, with pulse of 108. The injections were usually given every other day, sometimes daily, up to March 16th, at which time she had had thirty injections, only one of which had produced a chill. For two-thirds of the injections the filtered product was used, in one-third the unfiltered. The patient regained her normal weight and was in perfect health one and one-half years later, when she returned to her home in Europe.

CASE XVI.—*Small round-celled sarcoma of the lip. Patient well nearly nine years after disappearance under four weeks' toxin treatment.*—P. B. S., female, aged five years. Father a physician. Child always well. Mother first noticed a spot on the lower lip one and one-half inches below the mucous membrane, in July,

1896. This grew to the size of a pea, when it was removed by Dr. J. R. Yocom, of Tacoma, Washington, in September, 1896. The tumor was encapsulated and did not involve the mucous membrane. On the 25th of November there was evidence of a recurrence in the scar. On December 19th a large, V-shaped incision was made, removing the mass with considerable normal tissue on either side. On January 20, 1897, there was again evidence of a local recurrence. The patient was sent to me on February 4, 1897. At this time there was a tumor at the site of the old cicatrix, about one inch long, one-fourth inch wide, and extending nearly to the mucous membrane. The patient was treated with the mixed toxins, in doses of from two to seven minims, locally. After about

FIG. 11

Small round-celled sarcoma of lip. Recurrent. Disappeared under toxins. Well nine years.

four weeks the tumor disappeared and the tissues regained their normal appearance. The patient has remained well up to the present time, nine years.

CASE XVII.—*Recurrent spindle-celled sarcoma of the tibia. Amputation advised; preliminary trial of the toxin treatment; entire disappearance; patient well seven years.*—W. F., male, aged twenty-seven years; Canadian; farmer by occupation; family history good. In 1892 a small tumor was removed from the scalp. In 1896, a growth, the size of a plum, was removed from below the jaw. March 29, 1897, he noticed a swelling over the tibia of the left leg at about the junction of the middle and upper thirds; this slowly increased in size. On July 28th, operation by

Dr. Stewart, of Toronto. November 25th, of the same year, a second operation was done, consisting in incision and curetting of the bone; some of the tissue was sent to Dr. John Caven, Professor of Pathology at the University of Toronto, Canada, who pronounced it spindle-celled sarcoma. The tumor reappeared soon and the patient was referred to me on February 13, 1899, by Dr. Caven. Physical examination at this time showed a tumor at about the junction of the middle and upper thirds of the left tibia three by four inches in extent, with ill-defined border; over the central portion were two ulcerations, the size of a silver quarter. The patient was sent to the General Memorial Hospital and put upon the mixed toxins of erysipelas and bacillus prodigiosus for about two months. The tumor rapidly disappeared under the treatment; the bone cavity healed by healthy granulations. Before the healing process was entirely completed, the patient contracted a severe attack of accidental erysipelas (a fresh case of erysipelas had been in the ward not long before), running the usual course of about ten days. Healing continued rapidly and was completed two to three weeks later. The patient returned to his home in Chesley, Ont. He has been in perfect health ever since this time, seven years, and has been able to attend to his usual duties as a farmer.

Case XVIII.—*Spindle-celled sarcoma of chest wall; soft parts; eight times recurrent.* Dr. X., male, aged thirty-seven years. Very vascular, with extensive admixture of round cells. Toxins begun November 4, 1894, continued in small doses, with intervals of rest for three and a half years. Two or three small nodules removed in meantime. A small nodule was removed in November, 1902, from site of old trouble, under nitrous oxide gas. Microscopic examination still showed it to be spindle-celled sarcoma. This patient is a prominent surgeon, and has been able to attend a large practice and remains in perfect health at the present time, eleven years since the beginning of the treatment.

Case XIX.—*Spindle-celled sarcoma of parotid, with involvement of submaxillary and cervical glands. Recurrent, inoperable.* Mr. L., male, aged forty-one years. Referred to me in June, 1897, by Dr. J. W. Wright, of Bridgeport, Conn. The diagnosis of spindle-celled sarcoma had been confirmed by microscopic examination, and the case was quite inoperable. The mixed toxins had been tried for three weeks with little apparent improvement. The patient was admitted to my service at the Post-Graduate Hospital, and being in vigorous health the toxins were pushed to the point of producing seven chills, nearly every day. The tumor quickly showed marked improvement, and at the end of ten weeks had entirely disappeared. The patient remained well without any recurrence for more than six years, when he died very suddenly of gastric hemorrhage.

CASE XX.—*Very large. Recurrent. Inoperable fibro sarcoma of gluteal region and thigh. Recurrent.* Mr. S., aged thirty years. Large primary tumor removed two years before by Dr. Charles

FIG. 12

Spindle-celled sarcoma of parotid and neck. Recurrent inoperable. Disappeared under toxins. Well six years. Photograph taken after tumor had disappeared. (Case XIX.)

FIG. 13

Fibro-sarcoma of gluteal region. Recurrent Inoperable. Disappeared under toxins. Well twelve years. (Case XX.)

MacBurney, at Roosevelt Hospital. Local recurrence shortly afterward, with rapid growth. Admitted to my service Post-Graduate Hospital, 1893. Treated with the mixed toxins for three months

The improvement was very slow, and when the patient left the hospital shortly after there was a large tumor remaining. This slowly disappeared without further treatment. Five years later there still remained two small, hard movable masses at site of the large tumor. These I removed for microscopic examination, and they proved to be only pure fibrous tissue. The patient is still in perfect health, without any return thirteen years later.

CASE XXI.—*Round-celled sarcoma of dorsal spine.* Mr. G., aged twenty years. Diagnosis confirmed by Dr. Harlow Brooks, pathologist of the Bellevue Hospital. The tumor was of enormous size, involving the lower dorsal and upper lumbar vertebrae. The patient had lost about fifty pounds in weight, and there was so much pressure upon the spinal cord that there was total paralysis of the lower extremities, bladder and rectum, and he was so weak that he was unable to turn over in bed. Seen in consultation with Dr. V. P. Gibney, of the Montefiore Home, in February, 1902. The mixed toxins of erysipelas and bacillus prodigiosus were begun and continued by the house staff under my direction; daily injections were given up to the following May, and severe reactions, temperature of 103° to 104°, followed most of the injections. Patient began to show improvement, local as well as general, almost at once. By September he was able to get out on crutches. In November he was shown before the New York Surgical Society by Dr. John Rogers. At that time he had regained nearly his normal weight and got about very well with the aid of a cane. In February, 1903, one year after treatment, he was able to walk perfectly well without support of any kind, and his general health had become perfect. He was able to resume his former occupation.

This I believe to be the most remarkable result ever obtained from the use of the toxins. Fortunately, there can be no doubt as to the diagnosis, since the tumor was not only examined by well-known pathologists, but specimens of the tumor have been preserved. I have shown this patient before various medical societies the past two years. He remains in perfect health, four years after treatment.

CASE XXII.—*Round-celled sarcoma of femur involving the lower two-thirds of shaft.*—A. G., aged nineteen years. A swelling was first noticed in the lower portion of the femur in November, 1901. This gradually increased in size, being accompanied by loss of weight and deterioration of general health. Physical examination on February 5, 1902, showed a large tumor extending from the condyles of the left femur to the junction of the middle and upper thirds. There was a fusiform enlargement of the entire lower two-thirds of the femur. On the outer aspect of the thigh, about one and one-half inches above the joint, there was a soft, fluctuating area just covered by thin and reddened skin. There was slight impairment of the functions of the joint itself. An incision was made under ether into the fluctuating area, and two

or three ounces of clear serum, similar to that which is found in cystic degeneration of sarcomatous tissue, were evacuated. A curette was passed into the cavity of the bone and typically sarcomatous tissue removed. Microscopic examination by Dr. E. K. Dunham and Dr. B. H. Buxton, showed it to be a round-celled sarcoma. The patient absolutely refused amputation at the hip, which I strongly advised.

The X-ray treatment was tried entirely as an experiment, four exposures a week being given for a month, at the end of which time the circumference of the tumor had decreased one inch. The treatment was discontinued for two weeks, during which interval the tumor had again increased nearly an inch. The treatment was resumed, and at the end of another month the circumference of the thigh over the centre of the tumor was one inch less than the original measurement. The treatment was continued the entire summer to December, 1902. At this time the measurement of the left leg was the same as that of the right. There was still some thickening in the lower part of the femur. The old sinus, which had never healed after the exploratory incision, was enlarged under ether and carefully curetted. Examination of the tissues failed to show any trace of sarcoma. The patient had gained twenty pounds in weight, but towards the end of December, 1902, began to show signs of a metastatic tumor in the left pectoral region; this grew rapidly until it became about the size of a hand, when it was partially removed under ether anæsthesia; it was found to be very soft and highly vascular. Shortly after this, a large tumor, the size of a child's head, developed in the right iliac fossa, extending from the costal cartilages, down to the pelvis; it could be easily felt in the lumbar region. The local treatments with the X-ray in the femur and pectoral regions were continued, and in addition the mixed toxins of erysipelas and bacillus prodigiosus were begun. After a few weeks the large tumor in the iliolumbar region began to soften and break down, and on becoming completely fluctuating was opened posteriorly. A very large amount of necrotic tumor tissue was evacuated and the sinus was drained for about a year. While the tumor in the leg had apparently disappeared, there remained a marked thickening of the bone, and the sinus leading to the broken-down area persisted. Examination of several curettings failed to show any longer evidence of sarcoma. At the present time, four years after beginning of treatment, aside from the sinus in the leg, the boy appears to be in perfect health. There is at present no evidence of sarcoma to be found.

Case XXIII.—*Inoperable round-celled sarcoma of the chest wall, involving ribs.* G. C., aged sixteen years; enjoyed good health up to 1903, when he had an attack of what was considered to be pleurisy with effusion. He was aspirated, but the dulness over the chest persisted, and he rapidly lost flesh and strength.

He was sent south, without improvement, and in October, 1903, entered the Johns Hopkins Hospital, where he was operated upon for a supposed empyema. A large incision was made, revealing a necrosis of the eighth and ninth ribs, and behind these some gelatinous masses were found. These were partially removed and examined by Dr. Welch, who pronounced them round-celled sarcoma. The patient was referred to me, and on May 26, 1904, was admitted to the General Memorial Hospital, where for two months the toxins were regularly administered; in addition, he received X-ray treatment three times a week. At that time the patient was so weak that he could hardly walk. There was a mass about the size of a man's hand over the ribs, with an extensive sloughing area in the centre. The improvement was very rapid, and when he left the hospital in the fall of 1904 there was no trace of the tumor left; the patient had gained twenty-five pounds in weight and seemed in perfect health. He returned to his home in Canada, where his family physician had been instructed to continue the toxin treatment in smaller doses two to three times a week.

By the end of January, 1905, the patient returned to New York for examination, and there was evidence of a local recurrence, which at first again showed some improvement; after a few weeks, however, the tumor began to slowly increase in size in spite of large doses of the toxins and regular prolonged X-ray treatment. The patient slowly failed and died in October, 1905.

CASE XXII.—*Small round-celled sarcoma of the neck and tonsil. Entire disappearance in seven weeks under treatment with the mixed toxins of erysipelas and bacillus prodigiosus.*—H. M., aged thirty-two years; harness-maker by occupation; family history good. The patient was referred to me on October 17, 1905, by Dr. Arpad G. Gerster, of New York, as an inoperable case of recurrent, small round-celled sarcoma. The patient gave the following history:

"In about the middle of August, 1905, he noticed a swelling on the left side of the neck, just behind the sterno-mastoid muscle. At about the same time he also noticed an enlargement of his left tonsil; there was no pain at first, but as both tumors increased rapidly in size, they soon became painful. In the latter part of August, 1905, the patient was operated upon at St. Mark's Hospital by Dr. Carl Beck, who made an attempt to remove the tonsil tumor, as well as that of the neck; he found it impossible, however, to make a complete excision. The patient was immediately put upon the X-ray treatment every other day, and also received radium treatment externally and internally; the latter, however, had little, if any, influence in checking the rapid growth of the tumor. On October 13th, while under the care of Dr. Goldwater, at the New York Polyclinic, a portion of the tonsil tumor was

removed and examined by Dr. F. M. Jeffries, director of the Pathological Laboratory of the New York Polyclinic, and also by the Pathologist of the Practitioners' Laboratory, both of whom reported the tumor to be a small round-celled sarcoma. On October 17th, the time that I first saw the patient, physical examination showed the following condition: The left side of the neck was occupied by a globular tumor, about the size of half an orange; it extended from the angle of the jaw in front to the mastoid process behind and downwards nearly to the clavicle. Its consistence was about the same as that ordinarily found in round-celled sarcoma; the skin was not adherent. Examination of the left tonsil showed it enlarged to two to three times its normal size. The patient's general health had been but little affected. He was admitted to the General Memorial Hospital on October 17, 1905, and immediately put upon the mixed toxins of erysipelas and bacillus prodigiosus without any other treatment. Daily injections were given, alternating, one day into the tumor direct, the other, into the pectoral region. The highest dose given was seven minims; his temperature ranged between 99.5° and 103°. In less than a week there was decided decrease in the size of the tumor and increase in mobility. The diminution continued steadily until, at the end of six weeks, both the cervical and tonsil tumor had apparently entirely disappeared. The patient was shown before a meeting of the Harvard Medical Society on November 25, 1905, and before the New York Surgical Society in January, 1906. He left the hospital at the end of seven weeks, and although there were no visible remains of the tumor, the toxins have been kept up twice a week in the pectoral region, as a prophylactic against further recurrence.

It is interesting to note that the toxins used in this case, prepared by Dr. B. H. Buxton, of the Loomis Laboratory, were eight months old.

The remaining cases will be found in the tables that follow:

The successful cases in the hands of other surgeons have been carefully tabulated, but a few cases deserve somewhat fuller detail:

Case I.—*Round-celled sarcoma of the femur, too extensive for hip-joint amputation. Entire recovery; the patient perfectly well more than four years afterward.*—R. L., aged nineteen years; was admitted to the Mt. Sinai Hospital on May 24, 1898, and remained until July 24th, suffering from spontaneous fracture of the femur. The diagnosis of malignancy was not made until her re-admission on December 24, 1898, when it was found that there was a shortening of 2½ cm. The trochanter was two cm. above Nelaton's line, false motion in all directions. The upper and outer aspects of the thigh were occupied by a large swelling of semi-solid consistence. There was no tenderness. The patient's

Table of Personal Cases of Complete or Partial Success with Late Results

No.	Age	Sex	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
1	35	M	May 1891	Neck and Tonsil Recurrent Inoperable	Spindle Celled	Repeated Injection Living Cultures 4 mos. One attack of Erysipelas	Tumor nearly disappeared General health restored	Patient lived eight years and then died of recurrence
2	40	M	April 1892	Back and Groin Recurrence Inoperable	Mixed Celled Round and oval	Living Cultures of Erysipelas 4 attacks of Erysipelas Finally Toxins	Entire disappearance (vid text)	Patient remained well 8½ years then died of abdominal Metastasis
3	17	M	Jan. 1893	Abdominal Wall and Pelvis Inoperable	Spindle Celled	Mixed Toxins (filtered) Erysipelas and B. Prodigious	Entire disappearance in 4 mos. treatment	Patient in perfect health 13 years later
4	29	F	Oct. 1898	Abdominal Wall Inoperable	Spindle Celled	Mixed Toxins 3 mos. (Buxton)	Entire disappearance	Patient in perfect health at present, 12 years later
5	17	F	Jan. 1904	Leg Popliteal and Space Recurrent Osteo Sarcoma Foot	Spindle Celled	Mixed Toxins Buxton	Entire disappearance Recurred 1½ years. Amputation below Trochanter Recurred in Gluteal Region Finally disappered under continued Toxin treatment	Patient well Dec., 1905, 12 years from beginning of treatment, 10 years since end
6	34	F	June 1894	Chin, Lower Jaw Floor of Mouth Inoperable	Epithelioma (Microscopic Examination)	Mixed Toxins. 3 mos. Buxton	Entire disappearance	Patient well when last heard from 6 years later
7	16	F	June 1894	Chest Wall very extensive Inoperable	Spindle Celled	Mixed Toxins. 4 mos. Buxton	Entire disappearance	Patient well 1905, 11 years later
8	24	M	March 1904	Chondro Sarcoma of Ilium very large	Chondro Sarcoma	Mixed Toxins (Buxton)	Entire disappearance	Recurred 7 mos. later and finally proved fatal
9	24	F	Oct. 1894	Sarcoma Omentum Mesentery and Gall Bladder	Round Celled	Mixed Toxins. 5 mos. (Buxton)	Entire disappearance	Patient well January 1906 11 years

No.	Age	Sex	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
10	38	M	March 1895	Sacrum Inoperable	No Microscopic Examination, but Inoperable Tumor of Sacrum Examined by several surgeons	Mixed Toxins. 6 mos. Buxton	Entire disappearance in 3 mos. Patient gained 40 lbs. in weight	Patient well Jan., 1906, 10½ years later
11	30	F	1893	Gluteal Region	Spindle Celled	Mixed Toxins. 3 mos. (Buxton)	Entire disappearance	Patient in good health, no recurrence, Dec. 1905, 12 years later
12	40	F	Nov. 1895	Intra Abdominal Inoperable Size child's head	Spindle Celled	Mixed Toxins 3 periods of obout 2 months each	Tumor disappeared. Recurred and again disappered under further treatment	Patient in perfect health Dec. 28, 1905, 10 years later
13	16	M	Oct. 1893	Sarcoma Pharynx Inoperable	Spindle Celled	Mixed Toxins Unfiltered. 8 mos. (Buxton)	Entire Disappearance	Patient well when last heard from 6 years later
14	20	F	Feb. 18 1896	Hand	Spindle Celled	Mixed Toxins. 11 mos. Buxton	Entire disappearance in in 2 months	Recurred 2 years later. Yielded for a time to further treatment. Finally grew rapidly and proved fatal in another year
15	55	M	1893	Iliac Fossa	Round Celled	Mixed Toxins. 2 mos. Buxton	Entire disappearance	Patient well 1 year later when last seen
16	18	F	1897	Abdominal Wall	Spindle Celled	Mixed Toxins 31 injections Buxton	Entire disappearance	Patient well 1½ years later when she returned to Germany
17	59	F	1895	Breast Recurrent Inoperable	Round Celled Angio Sarcoma	Mixed Toxins. 6 mos. Buxton	Entire disappearance with exception of small Nodule which was removed for Pathological Examination	Patient well over 8 years No recurrence
18	37	M	1894	Chest Wall 8 times recurrent	Spindle Celled very Vascular	Mixed Toxins Filtered and unfiltered Buxton	Disappearance 2 or 3 small Nodules removed first 3 years	Patient in perfect health Jan., 1906, 12 years later
19	5	F	1897	Sarcoma Lower Lip 3 times recurrent	Small Round Celled	Mixed Toxins (Buxton) 6 weeks	Entire disappearance	Patient well 8 years later

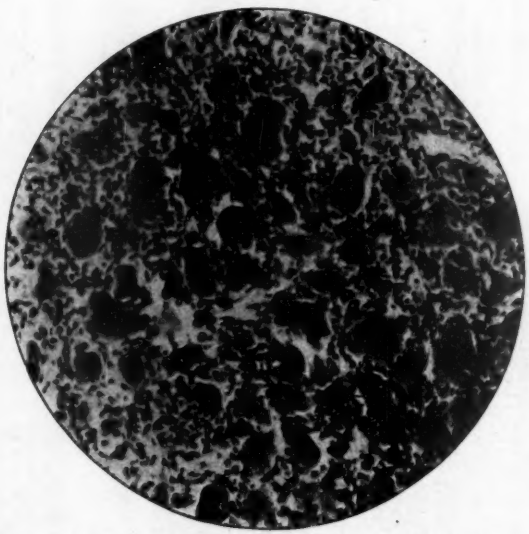
No.	Age	Sex	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
20	32	F	1897	Sarcoma Parotid 3 times recurrent	Mixed Celled	Mixed Toxins. 6 mos. Buxton	Disappearance except small Nodule excised. No longer traces of Sarcoma	Patient in perfect health with no recurrence Jan. 1906, 9 years
21	41	M	1897	Sarcoma Parotid Recurrence Inoperable	Spindle Celled	Mixed Toxins. 4 mos. Buxton	Entire disappearance	Patient free from recurrence 6 years afterward, when he suddenly died of Gastric Hemorrhages
22	35	M	Feb, 1898	Tibia Recurrent Inoperable except by amputation of Thigh	Spindle Celled	Mixed Toxins. 3 mos. Buxton	Entire Disappearance	Patient well at present, 8 years later
23	16	M	1897	Very large and Vascular	No Microscopic Examination Exploratory Loparatomy Dr. Geo. R. Fowler New York	Mixed Toxins Several mos.	Entire disappearance	Patient well 8 years later when he died of other trouble
24	44	F	1894	Spine Sarcoma Inoperable Recurrent	Spindle Celled	Mixed Toxins 2 mos.	Entire disappearance	Patient reported well 8 years later
25	52	M	Oct. 1900	Parotid Recurrent	Round Celled Microscopic Examination by Prof. W. H. Welch of Johns Hopkins	Mixed Toxins 9 mos.	Entire disappearance	Patient in perfect health 5½ years later
26	35	M	1902	Pectoral Region and Axilla Inoperable size of 2 fists	Round Celled	Mixed Toxins. 3 mos. Later Toxins and X-Ray	Nearly disappeared before X-rays began. Later all disappeared	Recurred 1 year later. Again disappeared. Recurred and finally proved fatal, Sept., 1905
27	8	M	1902	Back Recurred 3 times	Small Round Celled	X-ray at first failed, Mixed Toxins later	Entire disappearance	Patient well. No recurrence Jan 15, 1905, 3 years
28	38	F	May 1901	Abdominal Wall involving Bladder Wall	Fibro-sarcoma	Mixed Toxins 4 mos.	Entire disappearance	Patient perfectly well Jan., 1906 4½ years

No.	Age	Sex	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
29	16	M	Feb. 1902	Sarcoma Femur Lower Two-thirds with extensive multiple Metastasis	Small Round Celled	X-rays 8 mos. for Primary Tumor. Metastasis developed in Pectoral Region and Iliac Fossa Mixed Toxins nearly a year	Entire disappearance	Patient apparently free from Sarcoma in any region Jan., 1906 4 years
30	20	M	Feb. 1902	Spine Dorsal Very large	Round Celled Paralysis of Bladder and Rectum and Lower Extremities Loss of 60 lbs. weight	Mixed Toxins (Buxton) 4 mos.	Entire disappearance	Patient able to walk without crutches in 8 mos. and without cane in 1 year. Perfect health at present, 4 years later
31	56	M	Feb. 1904	Chest 3 times recurrant	Spindle Celled	Mixed Toxins Buxton and Parke, Davis	Partially removed by operation Disappeared entirely	Patient well without recurrence nearly 2 years
32	16	M	May 1904	Chest Wall Ribs and Pleura	Round Celled Very Vascular	Mixed Toxins and X-ray Buxton and Parke, Davis	Entire disappearance in 6 mos.	Recurred in 7 mos. and increased in spite of renewed treatment Death Oct., 1905
33	28	F	Oct. 1903	Intra Abdominal involving Mesentery size child's head	Small Round Celled Examined by Prof. W. F. Whitney, Harvard Medical School	Mixed Toxins (Buxton and Parke, Davis) with X-ray	Entire disappearance. Sudden high temperature with signs of Peritonitis. Development of Fecal Fistula. Recovery	Small mass felt other side of Abdomen 1 year later
34	34	M	Oct. 1905	Tonsil and Neck Recurrent size ½ orange	Small Round Celled	Mixed Toxins. Buxton (Toxins 8 mos. old) Injection Local and in Pectoral Region	Entire disappearance in 6 weeks. X-ray and radium previously tried and failed	Patient well at present
35*	42	F	1895	Breast and Pectoral Region Inoperable	Spindle Celled Microscopic Examination confirmed by Prof. W. H. Welch of Johns Hopkins	Mixed Toxins (Buxton) 78 injections (local)	Entire disappearance	Patient well Jan., 1906, 11 years later
36	18	F	1905	Tibia Recurrent twice	Round Celled	Mixed Toxins 5 mos. With X-rays part of time	Tumor disappeared	A small ulcer remained at last observation, Nov., 1905

*Note –In this case the treatment was carried out under my frequent direction by Drs. Storrs and Griswold, of Hartford, Conn.

general condition was only fair. January 5, 1899, operation by Dr. A. G. Gerster. An incision was made into the tumor which was found to be soft and intimately connected with the bones, apparently springing from the medulla of the femur. The tumor was considered inoperable, and a specimen was removed for pathological examination, and pronounced giant-celled sarcoma by Dr. Mandlebaum, the hospital pathologist. On January 25th the tumor was seen to have markedly increased in size and the patient was losing flesh and strength. The mixed toxins of erysipelas and bacillus prodigiosus were begun in initial doses of one minim,

FIG. 14



Round-celled (giant-celled) sarcoma of femur. Spontaneous fracture. Too extensive for amputation. Mixed toxins and curettings. Entire recovery. Well four years.

which were increased up to three minims, daily injections being given. The injections caused severe reactions, with pronounced chills and a temperature up to 105°. On February 28th, the injections were stopped temporarily. The glands in the groin at this time were markedly enlarged and the patient was much emaciated. The tumor was larger and sloughing. Examination on July 27th showed the tumor to have apparently slowly increased in size; it was still sloughing. On July 27th, hypodermic injections of sodium arsenate were begun in doses of five minims daily, and increased by one minim daily. The patient's general condition was worse, and she was transferred to the Montefiore

Home for Incurables. Shortly after this the tumor began to decrease in size; large masses of broken-down tumor tissue were discharged every few days. By May, 1901, the greater part of the tumor had sloughed away and the patient began to gain a little in flesh and strength. On May 29th, Dr. John Rogers, of New York, enlarged the opening, exposed the large bone cavity and removed considerable tumor masses by the curette, then packing the wound. On February 29, 1902, the wound was again enlarged and another curetting done by Dr. Elsberg. The bone cavity was filled with fluid iodoform paraffin wax and the greater part of the wound closed by interrupted sutures. The wound rapidly healed; part of the wax was discharged, but the greater part retained. From this time on the patient gained rapidly in flesh and strength. The tumor removed at the last operation was examined by a pathologist and showed no sarcomatous element, but only fibrous tissue. At this time there was fair union of the two fragments, and by the end of the year, perfectly firm union, so that the patient was able to walk without any support. The patient was shown before the New York Surgical Society by Dr. Rogers, in 1903, without any trace of recurrence and with perfect union. The specimen removed by Dr. Gerster at the original operation was examined by Prof. T. M. Prudden, of the College of Physicians and Surgeons, who prononnced it such a typical specimen of round-celled (giant-celled) sarcoma that he would like one for class demonstration.

Case II.—*Inoperable round-celled sarcoma of the upper jaw, with metastases, successfully treated with the mixed toxins.* Case of Dr. O. K. Winberg, of Lake Park, Minn. For a full history of this case, with pathological report by Dr. William H. Welch, of Johns Hopkins Medical School, see *New York Medical Record,* May 3, 1902. The following is a brief abstract:

A. Y., male, aged forty years, veterinary surgeon; was struck over the right superior maxilla by the horn of a bull in February, 1901. Pain and swelling developed not long afterward. In the middle of April the diagnosis of sarcoma was made. On May 9th, the patient was operated upon at St. Paul by Dr. C. K. Wheaton. An unsuccessful attempt was made to remove the entire growth which, at that time, involved the antrum and almost the entire upper jaw. The portion which it was impossible to remove, was curetted and cauterized. A mass, the size of a hen's egg, was removed from underneath the ear on the opposite side.

After a few days the growth began to increase in size very rapidly. The patient's local and general condition became steadily worse. He could hardly walk from the door to the carriage. Pulse 130; jaundice, which at first was but slight, had become very pronounced; there was dulness and tenderness in the hepatic

region. The tumor extended from the right malar eminence to the bridge of the nose, with which it was even in height, and downwards to the edge of the inferior maxilla. On August 12th, the jaundice was profound; liver much enlarged; pulse 140 to 150; speech was difficult to understand; the odor from the disintegrating portion of the tumor was almost unbearable. Upon the advice of Dr. G. D. Haggard, of Minneapolis, the mixed toxins of erysipelas and bacillus prodigiosus were begun by his physician, Dr. O. K. Winberg. The injections were made into the arm, beginning with a dose of one minim, and gradually increasing the same. Improvement, which was slight at first, became more and more marked. The jaundice had disappeared entirely at the end of three weeks. There was marked decrease in size, both of the primary tumor and the one in the left submaxillary region. The toxins were kept up until January, 1902; 103 injections in all were given. The patient's weight at the time of the beginning of the treatment was 113 pounds, being a loss of about fifty pounds from normal. The tumor entirely disappeared and the patient fully recovered his former health. He was exhibited by me at the Surgical Section of the New York Academy of Medicine, January 13, 1902. The patient has remained in perfect health up to the present time, four years later.

Case III.—*Dr. Howard Lilienthal's Case.* Man, aged forty-eight years; operated upon in 1901 for tumor of left seventh rib. Pleura involved and about an inch square of this tissue was removed together with about four inches of tumor including rib. Tumor was cystic and evidently sarcoma. The surrounding tissues were so involved that operation was abandoned and considerable cyst tissue left behind, especially in the ends of the excised rib. Wound sutured, the pleural defect packed. Healing prompt, but scar in a few weeks became thickened, especially at the ends. Examination of tumor by Dr. F. S. Mandlebaum, pathologist to Mt. Sinai Hospital, showed it to be "pigmented sarcoma." The injections with the mixed toxins were begun and continued for about eight weeks; they were given every three to four days, causing reactions of from 100° to 101.5°.

The man has remained perfectly well more than four years. Dr. Alfred Meyer, his physician, found an area about as big as a 25-cent piece in the right anterior axillary line over the seventh and eighth ribs, where there was fine crepitation on deep inspiration. This was discovered right after the operation and persisted until a few months ago, at his last examination. There is nothing palpable here or anywhere else. The patient was seen by Dr. Lilienthal in December, 1905, and appeared in perfect health.

Case IV.—*Extensive inoperable, intra-abdominal sarcoma, successfully treated with the mixed toxins.* Case of Dr. Herman

Mynter, of Buffalo; a full report of which may be found in the *New York Medical Record* of February, 1895. The patient was a girl, aged twelve years. There was a history of local injury two or three months prior to the development of the tumor in the abdomen. The condition of the patient when the treatment was begun was desperate. Diagnosis was confirmed by exploratory laparotomy, and microscopic examination of a portion of the tumor showed the growth to be a spindle-celled sarcoma. The tumor entirely disappeared and the patient, according to a letter from Dr. Mynter, dated May 25, 1898, is in good health at present. It is very important to note that this cure was effected through the systemic action of the toxins, all of the injections having been made in the thighs. The duration of treatment was six weeks; large portions sloughed off and came away through the abdominal incision.

CASE V.—*Inoperable epithelioma of uterus, or sarcoma, successfully treated with the toxins.* Case of Dr. R. M. Stone, Omaha. My former paper contained a brief reference to this case, which was subsequently published in full in the *New York Medical Record,* 1896. The patient, Mrs. B., aged forty-six years, had lost fifteen pounds in weight, the right broad ligament was markedly infiltrated. The disease had progressed so far that hysterectomy was not to be considered—three surgeons who had seen her in consultation, regarding the case as absolutely hopeless. The toxins were begun on December 6, 1895, and continued for two months with the result that the tumor, as well as the infiltration of the broad ligament, disappeared. The patient regained her usual health. Upward of one hundred sections of the tumor were examined by Dr. W. R. Lavender, Professor of Pathology to the Omaha Medical College, who made the diagnosis of spindle-celled sarcoma. Specimens of this tumor were very carefully examined by Dr. B. H. Buxton and Dr. E. K. Dunham, of New York, and their diagnosis was undoubted epithelioma. The patient remained well for three years, and then had a local recurrence which proved fatal.

CASE VI.—*Inoperable spindle-celled sarcoma of the uterus, recurrent; entire disappearance within nine months after the treatment was begun.*—Patient of Dr. H. T. Williams, of Rochester, N. Y. The patient, female, aged thirty-seven years, Canadian by birth, married nine years, no children. Menstruation began at sixteen, regular and normal in amount. Dysmenorrhea for past twelve years. The patient was first seen by Dr. Williams, April 16, 1891. The patient had noticed a growth in the abdomen six years before, since which time it had gradually increased in size. Her health was fair. Diagnosis: uterine fibroid. May 31, 1891, abdominal median incision. Large, smooth fibroid of uterus; sound passed nine inches. Numerous adhesions, in view of which latter

it was considered best not to do hysterectomy but to try the effects of spaying. Both tubes and ovaries, which were large and cystic, were removed as close to the uterus as possible. Catgut used to ligate pedicles. Recovery from operation without disturbance. November 21, 1901, menstruation more regular and much less profuse. Uterine sound passed five inches. May 19, 1892, periods every four weeks and almost normal in amount; sound passed four and one-half inches. Patient had been gaining flesh. She was then lost sight of until March, 1896, when she again came to Dr. Williams complaining of pain in right side, and saying that she felt another tumor. Examination showed a large, hard tumor about the size of two fists in right side of abdomen, and upon vaginal examination it appeared to spring from right horn of uterus. The tumor was not very movable and seemed to be attached to abdominal muscles. March 24, 1896, exploratory incision through abdomen revealed a large, elastic tumor apparently originating in right pedicle, extending into abdominal muscles and adherent to intestines. As operation would have had to be a very extensive one, involving the removal of a large amount of abdominal muscle with the growth and probably resection of the intestines, it was not deemed possible that the patient could survive it. A portion of the tumor was removed for microscopic examination, which showed it to be a spindle-celled sarcoma. The abdominal wound was closed with eight silver wire sutures and healed by first intention. The tumor increased rapidly in size, and a month after exploratory incision it projected several inches above the surface of the abdomen. April 24, 1896, three minims of the mixed toxins of erysipelas and bacillus prodigiosus were injected into the center of the tumor. The reaction was very great, patient had a severe chill, went into collapse, and brandy with strychnia, with salt solution per rectum and hypodermically, were required before she rallied, which she did a few hours later. Temperature had risen to 106°, but after a few hours had dropped to 100°, and next day was normal, but patient felt very much exhausted.

April 28, 1896, one minim of the toxins was injected into the tumor about an inch below the point of first injection. The symptoms of April 24th were repeated, but less severe, the temperature rising to only 103°. The patient declared she would rather die than have any more injections; however, she was finally persuaded to permit another injection of one minim of the toxins on May 1, 1896. Reaction was less severe, temperature reaching but 102°. On May 5th three minims were injected, causing a temperature of 103° and slight chill. On May 8th and 14th, three minims were given and were followed by considerable reaction, but temperature was not high. May 18, four minims were injected, causing a very severe prolonged chill and a temperature of 105.4°

F. The patient felt extremely weak for some days afterward. After each of the previous injections a slight erysipelatous blush had appeared around the point of injection, but disappeared in a few days. This time an area of three to four inches in circumference of bright red color appeared. Poultices were applied to it and in a few days it turned black in the centre and a slough about the size of a silver half dollar came away, leaving a hole of two to three inches in depth in centre of tumor. The patient positively refused to have any more of the toxins used. This opening discharged for several months, but the tumor grew rapidly smaller. Eight months later it had entirely disappeared. Dr. Williams wrote me in November, 1905, that she was in good health at the present time, more than nine years later.

FIG. 15

Case of Dr. C. L. Banks, sarcoma of parotid. Disappeared. Patient died eight years later of recurrence.

FIG. 16

Case of Dr. C. L. Banks.

CASE VII.—*Sarcoma of parotid gland. Inoperable.* Case of Dr. C. L. Banks, of Bridgeport, Conn. Mixed toxins injected for several months in 1896. Tumor slowly decreased in size until it entirely disappeared. The patient remained well for eight years, then had a recurrence which proved fatal.

All of the other successful cases deserve to be given in detail, but space will not permit. They are given in abstract in the accompanying tables. Many of them can be found in a former paper (*Journal of the American Medical Association*, August, 1898.)

TABLE OF SUCCESSFUL CASES TREATED BY OTHER SURGEONS

Name of Surgeon and Reference	No.	Sex Age	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
Herman Mynter Medical Record Feb., 1905	1		1895	Intra Abdominal involving Cæcum Omentum and Mesentery	Spindle Celled		Entire disappearance	Patient well 4 years later
L. L. McArthur Chicago Medical Recorder 1895, p. 120, and Personal Communication	2	F 31	1894	Sarcoma Calf Leg	Spindle Celled	2-3 months	Entire disappearance	Patient well 10 years
Ibid	3		1895	Sarcoma Radius	No Microscopic Examination Amputation of Arm advised by Christian Fenger	2 months	Entire disappearance	Patient well 3 years
Ibid	4	F 5½	1896	Sarcoma of Antrum and Naso Pharynx	Round Celled	3 months	Tumor disappeared Child gained in weight from 37 to 59 lbs.	Recurred a few months later and proved fatal
John E. Owens New Orleans Medical and Surgical Journal July, 1897	5		1896	Sarcoma Tibia	Round Celled (Giant Celled)		Entire disappearance	Patient well 8 years
Transactions New York Surgical Society Reported by Dr. John Rogers	6	21	1889	Sarcoma Femur below Trochanter Spontaneous Fracture Beyond Amputation	Round Celled Giant Celled Confirmed by Prof. T. M. Prudden	3 months	Entire disappearance Bone reunited	Patient shown to New York Surgical Society in perfect health 4 years later
Dr. Joseph Grindon St. Louis, Mo. Personal Communication	7	F 55	1897	Inoperable Spindle Celled Sarcoma Supra Clavicular	Spindle Celled		Entire disappearance	Recurred in Axilla in 9 mos. Removed Toxins again given Patient well 8 years
Dr. H. L. Williams Rochester, N. Y. Personal Communication	8	F	1896	Sarcoma Intra Abdominal	Spindle Celled	4 weeks	Entire disappearance vid text	Patient well 9 years

Name of Surgeon and Reference	No.	Sex Age	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
Dr. R. M. Stone Omaha, Neb. Medical Record, N. Y. Nov., 1896	9		1896	Uterus Inoperable very severe Hemorrhages	Epithelioma Reported as Spindle Celled Sarcoma. Exhaustive Examination proved it to be Epithelioma	3 months	Entire disappearance vid text	Patient remained well 3 years then died of local recurrence
Czerny V. Heidelburg Münchener Medinische Wochenschrift, 1895	10		1895	Parotid	Round Celled size of Fist	18 injections	Large Tumor reduced to small mass and removed by operation	Patient alive 1 year later, and well
Dr. Howard Lilienthal New York Surgical Society Transactions Annals of Surgery and Personal Communication	11	M Adult	1901	Sarcoma of Ribs	Round Celled	Mixed Toxins Parke, Davis & Co.	Entire disappearance	Patient well over 4 years
Dr. Chas. R. Barber Rochester, N. Y. Personal Communication	12	M 35	1894	Intra Abdominal very extensive Recurrent involving Mesentery and Omentum	No Microscopic Examination but Recurrent	Unfiltered Toxins (Buxton)	Entire disappearance	Patient alive and well 12 years later
Dr. Horace Packard Boston "Five Years in Surgery" and Personal Communication	13	F 39	Aug. 1895	Recurrent Parotid	Spindle Celled	Toxins, unfiltered (Buxton)	Entire disappearance	Patient well 2½ years later
Ibid	14	F 15	May 1896	Inoperable Sarcoma Pelvis	Endothelial Sarcoma Round Celled	Toxins, unfiltered (Buxton) few weeks	Entire disappearance	Patient well 2¾ years later
Ibid	15	F 55	May 1896	Inoperable Intra Abdominal Sarcoma	Spindle Celled	Toxins, unfiltered	Entire disappearance	Patient well 2 years later
Prof. J. Collins Warren Boston Boston Medical and Surgical Journal, Dec. 26, 1896	16	M Adult	1896	Neck Recurrent	Round Celled	Toxins, unfiltered (Buxton)	Entire disappearance	Recurrence 6 mos. later

Name of Surgeon and Reference	No.	Sex Age	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
Matagne H. Aoz Medical de Liege May 14, 1896	17		1895	Recurrent Sarcoma of Neck		Toxins, unfiltered 3½ months	Entire disappearance	Slight recurrence in 6 mos.
Ibid	18		1895	Recurrent Sarcoma of Neck size Fetal Head		Toxins, unfiltered 3 months	Decreased two-thirds	Died of shock following operation to remove the remainder
Mr. Moullin Mansell London Lancet. Feb. 5, 1898	19	M 28	Dec. 1895	Inoperable Sarcoma Iliac Fossa	No Microscopic Examination	Toxins, unfiltered 2 months (Buxton)	Entire disappearance	Patient well 2 years later
Ibid	20	M	Nov. 1896	Inoperable Sarcoma Iliac Fossa and Flank	No Microscopic Examination	Toxins, unfiltered several weeks	Entire disappearance	Patient well 2 years later
Ibid	21	M 28	Oct. 1895	Large Inoperable Tumor of Hip 4 months duration	Clinical Diagnosis Sarcoma	Toxins, unfiltered (Buxton) 2 months	Entire disappearance	Patient alive and well 1 year later
Dr. Sydney Wilcox N. Y. Journal of Homœopathy Jan., 1896	22	F 30	June 1895	Sarcoma of Left Forearm	Round Celled	Toxins, unfiltered 2 months (Buxton)	Entire disappearance	Well 3 mos.
A. Marmaduke Shield British Medical Journal Jan. 23, 1897	23	F 44	April 1896	Inoperable Sarcoma of Breast Recurrent	Round Celled	Toxins, unfiltered	Tumor disappeared by breaking down and sloughing	Staphylococcus Infection Pyæmic Death (Toxins Sterile)
Dr. R. Tilly Chicago Personal Communication	24	M Adult	Aug. 1894	Sarcoma Orbit Inoperable	Round Celled	Toxins, unfiltered (Buxton) 3 weeks	Tumor disappeared	Died suddenly 5 weeks later. Cause unknown
Dr. J. A. Moore Helena, Montana Personal Communication	25	M 31	April 4 1894	Sarcoma Mastoid size Goose Egg		Toxins, unfiltered 2-3 months (Buxton)	Entire disappearance	Patient well 2 years then local recurrence
Ibid	26	F 31	Jan. 1894	Supra Clavicular Multiple	Round Celled	Toxins, unfiltered (Buxton) 1 month	Entire disappearance	Recurred soon

Name of Surgeon and References	No.	Sex Age	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
Dr. J. A. Jackson and Dr. F. L. Lewis Transactions Central Wisconsin Medical Society 1897	27	F 36	Sept. 1896	Breast	Clinical Diagnosis Confirmed by Dr. Christian Fenger Chicago	Toxins, unfiltered (Buxton)	Entire disappearance	Died 1 year later with Metastasic Tumor in Rectum
Mr. W. H. Battie St. Thomas Hospital London Lancet. April 9, 1898	28	M 30	June 1897	Multiple Infra and Supra Clavicular and Pectoral Region and Axilla	Fibro-sarcoma Spindle Celled Microscopic Examination by Dr. Shattock	Toxins, unfiltered 4 months	Almost complete disappearance	Patient shown to Medical Society of London nearly 1 year later
Dr. T. H. Rumbold San Francisco Personal Communication	29	F Adult	Aug. 1894	Breast Recurrent	Round Celled	Toxins, unfiltered (Buxton)	Entire disappearance	Died of Internal Metastasis Confirmed by Autopsy
Prof. Kocher Theodore Bern Noted by Gluckmon	30	F Adult	1895	Recurrent Inoperable Pelvis		Toxins, unfiltered Prepared by Prof. Tobel, of Bern	Marked decrease in size	Began to increase again within 1 year
Dr. H. A. Ferguson Chicago, Ill. Personal Communication	31	Adult	1896	Sarcoma Tibia	Round Celled	Toxins, unfiltered	Entire disappearance	*Patient well 1906 10 years
Dr. D. B. Hardenbergh Middletown, Conn.	32	M 48	May 1897	Sarcoma Iliac Fossa attached to Ilium	No Microscopic Examination	Toxins, unfiltered (Buxton) 3 weeks	Entire disappearance	Patient well for 7 years when he died of other trouble
Dr. M. L. Harris Chicago, Ill. Personal Communication	33	F 31	Oct. 1897	Recurrent Inoperable Sarcoma of Ovary involving Rectum	Round Celled	Toxins, unfiltered M ¼ to 40 in Arm	Very marked improvement Tumor much smaller Final sloughing of entire Tumor	Died 1 month later from Septic Absorption from Sloughing mass
Dr. J. C. Walton Reidville, N. C. Charlotte Medical Journal May, 1898	34	F Adult	May 1895	Very large Sarcoma of Fibula Amputation of Thigh advised by Surgeons Refused by Patient	No Microscopic Examination	Toxins, unfiltered (Buxton) 2½ months	Entire disappearance	Patient well 3 years later

*NOTE—While paper was in press I received a letter from Dr. Ferguson stating that he had since learned that the patient had had Syphilis in his earlier life, and he thought the diagnosis was probably wrong. A previous history of syphilis does not make it impossible, or even improbable, that he may have had a sarcoma later in life. The tumor was pronounced sarcoma by the pathologist, and disappeared under the toxins.

Name of Surgeon and Reference	No.	Sex Age	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
Moullin Mansell Lancet. Feb. 5, 1898	35	F 29	Oct. 9 1896	Recurrent Sarcoma Superior Maxilla involving Orbit	Round Celled	Toxins, unfiltered daily, 5 weeks Local injections	Tumor disappeared by sloughing	Patient well 14 mos. later no local recurrence Possibly Metastasis recurred in Tibia
Dr. F. H. Zabrinskie Greenfield, Mass. Personal Communication	36	F 40	1896	Intra Abdominal Recurrent	Spindle Celled	Toxins, unfiltered (Buxton) 1 year	Tumor disappeared	Patient well 2 years later
Dr. John O. Roe Rochester, N. Y. Personal Communication	37	M Adult	May 1894	Recurrent Sarcoma of Neck and Tonsil	Adenosarcoma Round Celled	Toxins, unfiltered (Buxton)	Tumor improved rapidly Had almost entirely disappeared when	6 mos. later developed Erysipelas of Scalp which proved fatal
Rudoph Matas New Orleans and Dr. Yandell Philadelphia Medical Journal. March 11, 1899 and Personal Communication later	38	M 28	Nov. 1898	Very large Pelvo Peritoneal extending from Ribs to Ilium and Median Line in front to Spine	Clinical Diagnosis Too weak and emaciated for Exploratory Operation	Toxins 23 injections	Entire disappearance in 1 month Gained 12 lbs. in 3 weeks	Patient well at last report, 2 years later
O. K. Weinberg Lake Park, Minn. Medical Record, N. Y.	39	M 40		Recurrent Inoperable Superior Maxilla with every symptom of Abdominal Metastasis	Round Celled Diagnosis confirmed by Prof. Wm. H Welch, Johns Hopkins Prof. Jones Ewing, Cornell	Mixed Toxins injections in arm	Entire disappearance Perfect recovery of health	Patient alive and well 4 years later
Dr. J. C. Willy New Orleans, La. Personal Communication	40	F 40	1897	Uterus Mixed Celled Inoperable	Mixed Celled	Toxins, unfiltered with intervals for 4-5 years Local injections into Cervix	Large Tumor nearly disappeared Patient able to get about and do her regular duties	Patient went to Europe to live 6 years later
Dr. I. H. Hundly Prof. Gynecology University of Maryland ersonal Communication	41	F 40	1903	Uterus and Broad Ligament Inoperable Partly removed by operation	Mixed Celled Round and Spindle	Toxins, unfiltered, mixed Parke, Davis & Co.	Entire disappearance of Tumor	Patient perfectly well Dec., 1905, 2 years later

Name of Surgeon and Reference	No.	Sex Age	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
Dr. E. H. Robb Newton, Ia. Personal Communication	42	Adult	1895	4 times Recurrent Sarcoma Lower Jaw	Pronounced Sarcoma by Dr. Nicholas Senn	Mixed Toxins (Buxton)	Entire disappearance of Tumor	Well 8 years then Metastatic Tumor in Foot recurred twice then disappeared with Toxins. Well at present 1 year
Dr. O. C. Davis Augusta, Me. Personal Communication	43	Adult	April 1901	Mixed Celled Sarcoma of Neck Recurrent Large Round and Spindle Celled	Mixed Celled Large, Round Spindle	Mixed Toxins (Buxton)	Tumor ½ size of egg involving deep strictures of neck Entire disappearance	Patient well 4 years
Dr. Robinson Dansville, Va. Personal Communication and Transaction Southern Surgical and Gynecological Association, 1904	44			Round Celled Osteo Sarcoma Femur	Round Celled	Mixed Toxins (Buxton)	Entire disappearance	Well 3 years
Ibid	45		1899	Testis Operation Recurred in other Testis	Round Celled	Mixed Toxins	Entire disappearance	Well 4 years
Ibid	46			Tibia		Mixed Toxins	Entire disappearance	Well 6 years
Dr. O. W. Roberts Springfield, Mass. Personal Communication	47			Intra Abdominal Probably Retro Peritoneal size Child's Head	No Microscopic Examination Patient experienced much pain	Mixed Toxins Several months Parke, Davis & Co.	Entire disappearance Examined by Dr. Coley Oct., 1905	Well Dec., 1905, 4 years
Ibid	48		1899	Intra Abdominal Exploratory Laparotomy	Sarcoma confirmed by Microscopic Examination	Mixed Toxins	Entire disappearance	Well Oct., 1905, 5 years
Ibid	49			Intra Abdominal Exploratory Laparotomy	Sarcoma confirmed by Microscopic Examination	Mixed Toxins	Entire disappearance	Well over 3 years

Name of Surgeon and References	No.	Sex Age	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
Dr. R. W. Shearman Brooklyn, N. Y. Personal Communication	50	F 32	Mar. 1904	Sarcoma of Pelvis and Abdomen Extending nearly to Crural Arch	No Microscopic Examination Pronounced Inoperable Sarcoma Dr. L. S. Pilcher	Mixed Toxins Parke Davis & Co. several months	Tumor disappeared Broke down and found its way below Poupart's Ligament. Aspirated 1st 40 oz., 2d 18 oz. Broken down tissue	Patient well and doing own work Sept., 1905 1½ years later
Dr. George R. Fowler	51			Melanotic Upper Jaw Inoperable				Recurred 2 years later
Dr. Howard Lilienthal Transaction New York Surgical Society 1904, and Personal Communication	52	M Adult	1901	Ribs Inoperable Melanotic	Round Celled Melanotic	Mixed Toxins (Buxton)	Entire disappearance	Patient well 4 years
Dr. C. P. Chapin Buffalo, N. Y.	53	Adult	Jan. 1902	Thoracic	Round Celled	Mixed Toxins	Entire disappearance	Patient well 3 years
Dr. P. C. Boomer Chicago, Ill.	54	Adult		Chest and Nose size of Silver Dollar	Epithelioma	Mixed Toxins 1 month	Entire disappearance	Recurrence in 6 mos.
Dr. N. S. Hunting Quincy, Mass. and J. J. Thomas Boston Medical and Surgical Journal. Oct. 3, 1901	55	M Adult	1901	Myeloma of Spine	Myeloma of Spine involving Ribs	Mixed Toxins once or twice a week for 2 years Buxton and Parke Davis & Co.	Process checked Patient remained in good health 5 years, the longest known period of life with Myeloma, then died of other trouble	Patient in good health until April, 1905, when he died of acute Labor Pneumonia. (Autopsy)
Dr. C. L. Banks Bridgeport, Conn. Personal Communication	56	M Adult	1896	Sarcoma of Partoid and Neck Recurrent Inoperable	No Microscopic Examination Tumor size of two fists	Mixed Toxins (Buxton)	Entire disappearance	Patient lived 8 years and finally died of recurrence
Dr. H. B. Underset Toronto Personal Communication	57	M 22	Dec. 1902	Sarcoma Thigh	Spindle Celled	Mixed Toxins Parke Davis & Co. 2-3 months	Entire disappearance	Patient in perfect health when last seen, more than 2 years later

Name of Surgeon and Reference	No.	Sex Age	Date	Locality	Type of Tumor	Treatment Duration	Result Immediate	Result Final
Ibid	58	F Young Adult	1902	Mastoid Region Recurrent	Spindle Celled	Mixed Toxins and X-ray Parke, Davis & Co.	Partial operation with Toxins immediately after Two doses gave very severe rigors Discontinued and X-ray used alone	Patient in perfect health at present, 2 years later
Dr. J. Babat Blake · Boston Personal Communication	59	Adult	1899	Humerus involving Coracoid Process and Glenoid Cavity of Scapula	Round Celled Osteo Sarcoma	Mixed Toxins several months Parke, Davis & Co.	Preliminary operation removed Head of Humerus, Tip of Carocoid Process and part of Glenoid Cavity	Examined by Dr. Blake 4 years later Patient in perfect health doing housemaids work Gained 10 lbs. weight
Dr. H. H. Beach Boston, Mass. General hospital case Personal Communication from former House Surgeon	60	Adult	1900	Ilium Very large	Osteo Sarcoma Spindle Celled	Mixed Toxins Parke, Davis & Co.	Entire disappearance	Well when last seen over 1 year later

In closing I desire to tender my most sincere thanks to Dr. William T. Bull for most generous help and encouragement, especially during the earlier and more trying inoculation experiments, which alone rendered the subsequent investigations possible. I also wish to thank Dr. Alexander Lambert for valuable aid in the preparation of the first toxins. I am under especially heavy obligations to Dr. B. H. Buxton, not only for placing at my disposal his knowledge and skill as a bacteriologist, but also for having given me his hearty co-operation during the past thirteen years. Whatever of value has come from these investigations to him belongs a large share.

TREATMENT OF SELECTED CASES OF CEREBRAL, SPINAL, AND PERIPHERAL NERVE PALSIES AND ATHETOSIS BY NERVE TRANSPLANTATION.[1]

WITH THE REPORT OF A CASE OF ATHETOSIS BENEFITED BY OPERATION.

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REMARKS BY DR. SPILLER.

A NEW field seems to have been opened in the treatment of selected cases of paralysis, whether they are of cerebral, spinal, or peripheral nerve origin, and also in the treatment of athetosis. It is not too much to say that the results obtained in cases of acute anterior po'iomyelitis by nerve transplantation have been o encouraging that the operation for recovery from the paralysis in selected cases of this disorder may now be regarded as passing beyond the experimental stage.

Acute anterior poliomyelitis is a disease of a more or less limited number of nerve cells in the anterior horn or horns of the spinal cord. In 1902 it occurred to me that we should be able by nerve

[1] The paper was read and the patient was exhibited before the College of Physicians November 1, 1905.

transplantation in acute anterior poliomyelitis to bring diseased peripheral nerve fibres into union with healthy nerves and thereby to restore function. Such a procedure would be more advantageous than a tendon transplantation, as by the former method the paralyzed muscles would be restored if the operation were successful. The subject has been discussed in a paper by Dr. Frazier and myself,[1] read before the American Medical Association.

In 1902 I suggested to Dr. C. H. Frazier and Dr. J. K. Young that we might with propriety try nerve transplantation in cases of acute anterior poliomyelitis where the palsy was not very extensive. The operation was performed on December 4, 1902, by Dr. Young, and the patient was exhibited by Dr. Young and myself before the Philadelphia Neurological Society February 24, 1903, and the case was reported in the *Journal of Nervous and Mental Disease*, in the proceedings of the Society, June, 1903. Even in February, 1903, some return of power could be observed, and at the present time the improvement is distinct. The case has been reported by Dr. Young before the American Orthopædic Association June, 1904, and also in a paper by Dr. Frazier and myself,[2] together with the report of another case in which the operation had been done by Dr. Frazier almost at the same time.

The chief dangers in operating on cases of anterior poliomyelitis are delayed union and overgrowth of connective tissue in the nerve at the site of operation. Where a whole nerve is diseased and is so large as the peroneal, it is probably necessary to cut a portion of the sound nerve used for grafting, either transversely or transversely and longitudinally, and when the latter is done to insert the split portion into the diseased nerve; but where the fibres are small, as are those supplying the anterior tibial muscle, probably a sufficient number of nerve fibres are cut in the healthy nerve by the longitudinal splitting and the insertion of the diseased fibres within the slit. The new axis cylinders which develop after an injury of nerve fibres are more numerous than those existing before the operation, and probably by growing into the diseased nerve, if we accept this view of regeneration, suffice for its innervation. If we accept the peripheral theory of regeneration, the axis cylinders that develop in the peripheral end of the nerve are sufficient for the restoration of function. It hardly seems advisable to cut a healthy nerve entirely across, as Kilvington suggests, because if an excessive amount of connective tissue forms reunion with functional restoration of the formerly healthy fibres may not occur.

Peckham,[3] as I found later, cut two of the four branches passing from the internal popliteal nerve into the heads of the gastrocnemius in a case of anterior poliomyelitis of ten years' duration and inserted them into the diseased nerve. At the end of six weeks

[1] The Journal of the American Medical Association, January 21, 1905.
[2] Loc. cit.
[3] The Providence Medical Journal, January, 1900, p. 5.

the toes could be extended (dorsal flexion) until they were perfectly straight, a motion that had been impossible until after this operation. There was no apparent weakness in the gastrocnemius and soleus muscles. The same operation was performed in another case for paralysis resulting from fracture of the spine. The results were not very gratifying in either case, and his paper seems to have received little or no attention.

The paralysis in cases of acute anterior poliomyelitis is often confined to a small group of muscles, as shown in a recent paper by Walther Baumann.[1] Baumann examined 85 cases of acute anterior poliomyelitis. Complete paralysis of one or both lower limbs occurred in 16 cases; complete paralysis of the lower limbs, except that the movement of the toes was preserved, in 5 cases; complete paralysis of the lower limbs, except that the movements of the extensor digitorum communis and the peronei were preserved, in 1 case.

Paralysis of only the	dorsal flexors of the foot	occurred in	29 cases.
" "	extensors of the knee	"	12 "
" "	peronei	"	10 "
" "	calf muscles	"	8 "
" "	flexors of the knee	"	8 "
" "	tibialis anticus	"	7 "
" "	glutei	"	6 "
" "	adductors	"	2 "

Complete paralysis of one or both upper limbs occurred in 3 cases; complete paralysis, except that the movements of the fingers were preserved, in 2 cases.

Paralysis of only the	deltoideus	occurred in	8 cases.
" "	flexors of the forearm	"	5 "
" "	thenar eminence	"	5 "
" "	pectoralis major and supinator longus	"	3 "
" "	triceps	"	4 "
" "	small muscles of the hand	"	2 "
" "	supraspinatus	"	2 "
" "	entire musculospiral territory	"	1 "

From this table it will readily be seen that partial paralysis is very common in anterior poliomyelitis, and especially noteworthy is the large number of cases, 29, in which the dorsal flexors of the foot were paralyzed. It is probably because of this that attention has been directed chiefly to the lower limbs as regards nerve transplantation in acute anterior poliomyelitis. The paralysis of the upper limbs, however, is amenable to treatment by nerve transplantation.

Hackenbruch[1] reported at the meeting of the Kongress der Deutschen Gesellschaft für Chirurgie, June, 1903, and therefore after the presentation of the case by Dr. Young and myself in

[1] Monatsschrift f Psychiatrie und Neurologie, June, 1905, p. 485.

[2] Archiv f. klin. Chirurgie, 1903, No 3, Bd. lxxi. p. 633; also Deutsche med. Wochenschrift, June 22, 1905, No. 25, p. 986.

February, 1903, that he had inserted a third of the tibial nerve into the paralyzed peroneal nerve in a case of poliomyelitis. In June, 1905, he reported the results obtained in this case and in two others. Two cases were only partially successful, but the third gave most gratifying results.

This third case was one of peroneal palsy, and the palsy seems to have been complete in the distribution of the peroneal nerve. A third of the posterior tibial nerve was inserted into the peroneal. Slight improvement was seen four months after the operation, but a year and a half after the operation the movements of the lower limb and foot were good, the patient was able to elevate herself upon the toes of this foot, and to stand on this foot alone. The limb had become 1 cm. longer and the foot had become larger. The limb, as a whole, was a little weaker than the other.

Many experiments have been performed in nerve transplantation on animals since the first operation by Flourens. Basil Kilvington[1] gives a very good presentation of this subject, and then makes an application to surgery. He suggests that nerve transplantation might be used in cases of anterior poliomyelitis, although he acknowledges that he has not performed the operation on the human subject. As he makes no reference to the work of others in so far as it relates to man, he was probably ignorant of the results already accomplished in cases of anterior poliomyelitis. His suggestion is to suture the nerve supplying the paralyzed muscles on to the cut surface of the proximal end of an adjacent healthy nerve. The healthy nerve may be cut partly across and the paralyzed nerve fixed in the gap so formed, or the healthy nerve may be cut completely across and its own peripheral end, as well as the peripheral end of the paralyzed nerve, may be sutured to the central end. This hardly seems a wise proceeding to me. Kilvington published his paper April 29, 1905.

Harris[2] and Low reported before the Clinical Society of London, October, 1904, a case of infantile paralysis in which they had done nerve suture in order to overcome paralysis of the right deltoid and spinati muscles. The operation is described by Harris in an abstract as follows (the original paper I have not as yet been able to obtain[3]): The fifth cervical nerve was split in halves, and the upper bundle, which caused no muscular contraction on faradic stimulation, save fibrillary movements in the deltoid, was cut across as near the foramen as possible, and turned down in front of the remaining half of the fifth nerve and then sutured into a nick cut in the front of the sixth cervical nerve. The uncut portion of the fifth nerve contained the fibres for the biceps, as faradic stimulation of this bundle caused powerful flexion of the forearm. In this way the degenerated bundle in the fifth nerve, supplying the deltoid, was

[1] British Medical Journal, April 29, 1905, p. 935.
[2] The Practitioner, August, 1905, p. 228.
[3] I have, since our paper was read, obtained the original article by Harris and Low.

sutured on to a healthy nerve so as to allow regeneration to take place by the formation of a connection with the healthy fibres in the sixth nerve. For sixth months after the operation no sign of improvement appeared, in spite of regular massage and galvanism. Then, eleven months after the onset of the paralysis, slight improvement in the power of the shoulder was noticed, and the progress, at first slow, afterward more rapid, was maintained, so that ultimately the child could put up her arm readily straight above her head.

It is therefore true, I think, that the operation of nerve transplantation for acute anterior poliomyelitis where the paralysis is not too extensive is passing beyond the experimental stage. The application of nerve transplantation to peripheral nerve palsies is apparent.

In most cases of hemiplegia the paralysis is greater in the extensors of the upper limb and in the flexors of the lower limb, but, as a rule, the difference is not sufficiently marked to justify the operation of nerve transplantation. Occasionally, however, the palsy is much more intense in certain muscles. Fischer[1] recently, in speaking of this subject, states that the weakness of the extensors of the fingers in rare cases of cerebral lesion may be so pronounced that the paralysis may have the appearance of musculospiral palsy, as in the cases of Pick and Oppenheim. I have observed a distinct difference in the degree of paralysis in the extensor and flexor groups of muscles in a number of cases in which hemiplegia had developed early in life.

It has been my endeavor for several years to devise some method of treatment for athetosis. This condition is observed only when some return of function has occurred, or at least when the paralysis is incomplete, and if the movements are violent the muscles hypertrophy because of their constant use; the patient with severe athetosis, however, has little or no voluntary control of his limbs, and the flexors are usually much more powerful than the extensors in the upper limbs. It occurred to me that if we could switch off, so to speak, some of this excessive innervation of the flexors into the extensors by nerve transplantation, we might be able to establish a more nearly normal relation between certain groups of muscles and their opponents, and by division of nerves be able to lessen the athetoid movements probably permanently. It hardly seemed likely that restoration of function would be so perfect as to permit a return of athetoid spasms. This subject was presented by Dr. Frazier and myself[2] in a paper read before the New York Neurological Society, March 7, 1905. At that meeting Dr. G. L. Walton remarked that in a case coming under his observation the athetosis was so troublesome that the arm was amputated at the shoulder at the request of the patient.

A case of extremely violent athetosis has been under my care

[1] Monatsschrift f. Psychiatrie und Neurologie, August, 1905, p. 98.

[2] Journal of Nervous and Mental Disease, May, 1905, p. 310; Walton, ibid., October, 1905, p. 655.

about five or six years at irregular per ods. The young man had probably had the movements all his life, except possibly during his first year, and had no control over his powerful muscles. His mother had been obliged for years to dress him with the greatest difficulty every morning. His upper limbs were jerked about most violently, but the flexor muscles were far more powerful than the extensors. The case seemed most suitable for an attempt at nerve transplantation, and was referred by me to Dr. Frazier for this purpose. The method of operation will be described by Dr. Frazier.

FIG. 1

Photograph taken before the first operation, indistinct despite the fact that it was instantaneous. It shows how constant and uncontrollable were the athetoid movements and shows also the intensity of the spasms. Much of the blurring of outlines has been removed in the reproduction.

The case was presented at the meeting of the American Neurological Association, June 2, 1905, two months and a half after the first operation, and at that time there was distinct return of power at the wrist, in the flexors of the fingers, and at the e bow, but the movements were by no means normal. The presentation was made at that time in order that the many neurologists present might be able to judge for themselves of the degree of athetosis that had existed before the operation, inasmuch as the right upper limb had not been operated upon at the time of the presentation; and

in order that the developments of the case, whatever they might be, could be watched. We made no claims—nor do we now—but presented the results of a hitherto unattempted operation for the relief of a most distressing condition, believing that, whether failure or success were the ultimate outcome, the results should be made known.

As early as two and a half months after the operation the condition of the patient was so much improved that he was well satisfied with the results, and stated he had never in his life been so comfortable. We had established at that time that it was possible to remove the athetosis if we caused a partial paralysis,

FIG. 2

Instantaneous photograph taken before the first operation, showing the violence of the spasms.

and we could argue that should the athetosis return it would do so only with the disappearance of the paralysis. In case of return of athetosis we should be able to diminish the voluntary power, and thereby also the athetosis, by some other operation.

It may be said that the operation was an attempt to influence a cerebral lesion by disturbing peripheral nerves, and this indeed is what it was. We could not remove the source of the irritation, but if we could remove the manifestations of this irritation without causing the patient more discomfort, we might consider the operation a success. This is what we have accomplished, at least in part. There is no doubt that this man's condition is far better

than it was before any operation was attempted, and we may hope for a still greater restoration of power. He has now returned to his occupation of selling papers and is very happy over his improved condition.

Massage and electricity have done much to keep up the tone of the muscles, and the patient has made frequent attempts to employ his upper limbs. He is now being treated by systematic gymnastic exercises.

Seven and a half months have passed since the first operation, and the results are most encouraging and lead us to believe that athetosis will not return, or if it should, that it will be far less severe than before the first operation. It is important to have established that with partial paralysis, produced by operation on nerves, athetosis disappears. No one, I think, who was familiar with this man's condition before any operation was performed, and sees him now, would dispute that he is far more comfortable than at any previous period of his life.

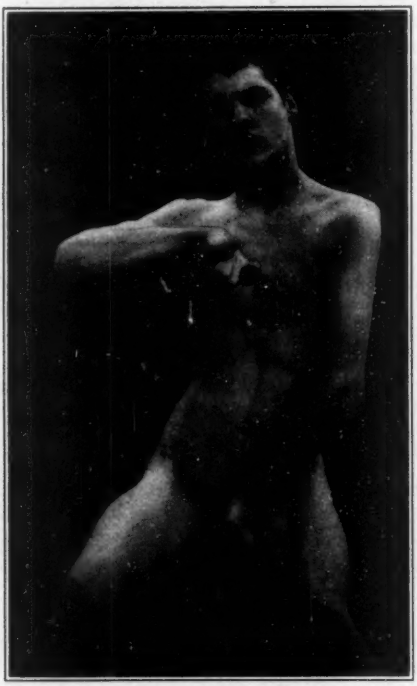
If athetosis is the result of irritation of central motor fibres it seems strange that no symptoms are produced by the prevention of any manifestation of this irritation. One might suppose that the impulses sent over the motor tracts, having been arrested, would flow over into fibres destined for the innervation of the lower limbs, or that some evidence of discomfort would be observed. Nothing of the kind occurred. It is said that sometimes in epilepsy, when the convulsion is arrested, the patient's condition is worse than if the convulsive seizure had freed the stored-up energy, and we might expect a somewhat similar result when the irritation of athetosis finds no outward expression, but such does not seem to be the case.

Dr. Purves Stewart recently suggested to me, after seeing the patient, that if in epilepsy we could cut all the motor nerves we should arrest the convulsions and produce a condition similar to that seen in our patient so far as arrest of involuntary movements is concerned, but we should not cure the epilepsy. I fully agree with him in this statement, but if we have arrested the athetoid movements, even though we have not removed the cerebral lesion, we have accomplished much. Epilepsy is more than convulsions, but if it were a practical operation to cut the nerves for the prevention of spasm, which of course it is not, we might resort to it.

The operation performed in this case of athetosis shows convincingly that when the peripheral end of a healthy nerve is inserted into another healthy nerve by a longitudinal and not transverse incision in the latter, return of function may occur in the inserted nerve. The musculospiral nerve was not cut transversely, and yet partial return of function has occurred in the distributions of the median and ulnar nerves. The results justify the end-to-side anastomosis—the peripheral end of the affected nerve inserted into

the unaffected nerve—we have advised for the treatment of the paralysis of anterior poliomyelitis confined to one or two muscles. There is unquestionably a difference between using the peripheral end of a healthy nerve and the peripheral end of a diseased nerve, but if the nerve is much affected it is not likely to regenerate by any method of transplantation, and it is because of this that the prognosis is better the earlier the operation is done. This method of end-to-side anastomosis, however, would probably not be advisable in those cases in which the entire nerve distribution such as

FIG. 3



Photograph taken soon after the first operation, showing the immediate paralysis of the left upper limb and marked athetoid movements of the right.

the peroneal, were affected, and it would probably be necessary, under such circumstances, to insert some healthy fibres into the diseased nerve.

The experimental operations noted below were performed at the suggestion of Drs. Spiller and Frazier under the direction of Dr. Van Kaathoven. The two cases cited are chosen as representative of a series of similar experiments giving similar results. This experimental work was done partly to demonstrate certain ques-

tions regarding restoration of function and the operative technique, and was performed in connection with the voluntary course in operative surgery.

CASE I.—Mongrel dog. Operation. An incision was made on the anterior aspect of the thigh over the femoral vessels and the anterior crural nerve exposed and freed. A posterior incision half way between the great trochanter and tuberosity of the ischium was then made, the muscles separated, and the sciatic nerve exposed and freed. An opening was then made through the adductor magnus, this perforation allowing of communication between the

FIG. 4

Photograph taken July 14, 1905, 120 days after the first operation, showing flexion of the forearm on arm as an evidence of gradual restoration of voluntary movements.

anterior and posterior aspects of the thigh. The two nerves were then cut. By means of silk sutures through the sheath the peripheral portion of the anterior crural was sutured to the proximal part of the sciatic, and the peripheral sciatic to the proximal anterior crural. The leg was then partially immobilized, the superficial wounds having been closed by means of silkworm sutures. Result: six days after operation the wounds were examined and found to have united by first intention. Stitches and bandage were removed. During the middle of the second week the dog commenced to move the injured leg. At the beginning of the third week restoration of function became more marked. It was observed that when walking

the animal extended its hind leg instead of flexing it. After three or four unsuccessful attempts at walking on the injured foot the animal apparently became discouraged and let the leg hang down, scampering away on three legs. About the onset of the fourth week the dog had apparently learned to control the movements of the hind leg, although when running he still frequently extended the leg instead of flexing it. During the latter part of the week the animal had improved markedly in its locomotion, the only defect being a turning under of the foot, apparently due to inability to extend it freely. At the end of the fifth week he showed marked improvement in this condition, now only turning the foot under occasionally, apparently only when running or excited. During

FIG. 5

Photograph taken July 14, 1905, 120 days after the first operation, showing flexion of th hand on the forearm as an evidence of return of voluntary movements.

the sixth and seventh weeks the animal practically walked as well as before section of the nerves. The results of this experiment were exactly similar to those of earlier ones, the same operation having been performed.

CASE II.—Terrier. A similar operation was performed upon the brachial plexus. The nerves being reached by a transverse section of the pectoralis major and a separation of the fibres of the pectoralis minor. The median and musculospiral nerves were chosen for the experiment. Suturing was done as before—peripheral median to proximal musculospiral and proximal median to peripheral musculospiral. Aside from some superficial suppuration the dog made a good operative recovery. No restoration of

function followed operation for eight weeks. There was some contracture at the elbow joint, none at the wrist. After fourteen to sixteen weeks there was less contracture and less atrophy, still the dog seemed to make little or no use of its leg. The explanation of failure in the cases of experimentation on the brachial plexus lies probably in the fact that the undivided nerves, the ulnar and musculocutaneous, cause spasm of the muscle groups governed by them, as the groups innervated by the median and musculospiral are temporarily paralyzed.

HISTORY OF A CASE OF ATHETOSIS.

BY DR. FRAZIER.

Frederick H., aged nineteen years, was admitted to the University Hospital on the 10th of March, 1905.

Social History. Single, native of Philadelphia. More than an average consumer of tea and coffee. Occupation, sells newspapers.

Previous Medical History. He was said to have been born at the seventh month. Had pertussis in childhood. For the past year has complained of rheumatic pains in the right leg, which have gradually grown worse. Apart from this he has always enjoyed good health.

Family History. Father and mother both complain of rheumatism; the former is believed to have some disease of the kidneys. Three brothers and sisters are living and in good health. There is no tuberculous, cardiac, neoplastic, or neurotic history in the ancestry.

History of Present Condition. The patient says that when he was eight months old he fell from a hammock, alighting on his back, and that he was unconscious for two hours. Nothing, however, abnormal was noticed about the patient until he was two years old, when he was taken to the Jefferson Hospital because of the beginning athetoid movements of his hands and arms, and also because of his inability to walk. His mother was told that nothing could be done, and that his condition was not the result of the accident. From the ages between two and twelve his movements became more exaggerated and there seemed to be some disturbance in speech. He did not learn to walk until he was twelve years of age. He then slowly improved in gait until the present time. Owing to weakness in his ankles and knees and the athetoid movements of his upper extremities he frequently fell down. He had been under the care of Dr. Spiller for several years at the Polyclinic and University Hospitals and later during a part of his stay at the Philadelphia General Hospital.

While in the surgical wards of the Philadelphia General Hospital a craniotomy was performed and the cortical centre for his left

upper extremity was excised. During his convalescence from this operation he had two or three convulsions, in which he lost consciousness at times for ten minutes. Since the operation his left arm has been more rigid, the pain in his right arm has been more pronounced, and his condition has grown steadily worse. The athetoid movements are very much more marked during excitement and cease entirely during sleep.

Physical Examination. Urine analysis: acid reaction; specific gravity, 1032; no albumin, no sugar; small amount of mucoid precipitate. Microscopic examination negative.

FIG. 6

Photograph taken July 14, 1905, 120 days after the first operation, showing the partial flexion of fingers as evidence of gradual restoration of voluntary movements.

Athetoid movements are not observed in the face, and the cranial nerves are not affected.

The upper limbs are in constant violent spasm and present intense athetoid movements in all parts. The flexor spasms predominate over the extensor spasms, and the hands are flexed forcibly on the forearms, and the forearms on the arms. From time to time either limb is drawn upward and backward at the shoulder, and sometimes the entire limb is drawn behind the trunk and held in this position a minute or two. In removing the coat of the patient great difficulty is experienced because of the violent spasms. The muscles of the upper limbs are unusually well developed as a result of the spastic movements, and yet the patient has not the slightest

control over the upper limbs. Any attempt on his part to perform a voluntary movement with his upper limbs increases the athetosis in an extreme degree.

The lower limbs are somewhat spastic, but not sufficiently so to prevent walking. His gait is awkward and stiff because of the marked tonicity of the muscles, but athetoid movements are not observed in these limbs.

March 16, 1905. First operation on the left extremity—lateral anastomosis of the divided median and ulnar nerves to the musculospiral nerve.

17*th*. Patient complains of pain, the result of involuntary contraction of triceps and coracobrachialis. The patient can extend the fingers and the hand on the wrist.

FIG. 7

Photograph taken in December, 1905, showing the voluntary power in raising the left upper limb at the shoulder and in flexing the left forearm on the arm.

18*th*. Wound dressed and rubber tissue drain removed. Plaster-of-Paris dressing reapplied. Convulsive movements of the left arm are not so pronounced as before the operation. There is no evidence of restoration of sensation in the distribution of the median nerve.

21*st*. Patient rests quietly the greater part of the time, and is kept in bed because that position is conducive to quietude. The wound is running an aseptic course.

31*st*. Involuntary movements are chiefly, if not entirely, in the muscles of the shoulder, especially in the deltoid and biceps; sensations for touch and pain are present over the front and back of forearm, but not so acute as in the corresponding parts of the right

arm. There is some involuntary movement of the triceps and at the left wrist. Sensations for touch and pain in the palmar surface of the hand are lost. They are present in the dorsal aspect of the hand, but only to a limited degree.

April 8th. Patient feels greatly benefited by the operation. It is probable that a subsequent operation will be performed, directed toward controlling the athetoid movements of the shoulder muscles.

17*th.* Second operation on left upper extremity performed by Dr. Van Kaathoven. The circumflex and musculocutaneous nerves were divided and an end-to-end anastomosis effected between the central end of the one and the distal end of the other, and *vice versa.*

22*d.* The patient has been very much more comfortable since the last operation. The muscles of the shoulders do not contract as violently as before, but there still seems to be a marked tendency toward extension in the forearm.

24*th.* There is some involuntary jerking on the radial side of the forearm, but this movement is slight and is in the supinator longus muscle. Involuntary movements around the shoulder have ceased. The patient seems to have no sensation for touch or pain in the palm of the hand, although it is present to some extent on the dorsal surface of the hand.

May 5th. There is very little jerking of the left upper limb, and what involuntary movement is seen is chiefly in the supinator longus muscle. The whole limb is somewhat spastic. There is considerable voluntary movement at the wrist and he can flex and extend the hand, especially when he is not excited. He can partially flex all the fingers, and the flexion is greater in the fingers nearer the ulnar side. Attempts at voluntary movements of the left hand increase greatly the athetosis of the right upper limb. The muscles of the left hand are somewhat wasted. Sensation has not returned at all in the palm of the left hand. Sensations of touch and pain are present in the left forearm anterior aspect, but diminished in the posterior part of the left forearm and left hand. Some sensation is felt in the dorsal aspect of the ulnar distribution of the hand, but none on the palmar surface of this nerve supply.

Dr. C. S. Potts reported that on this date he could detect no reaction in the muscles supplied by the ulnar and median nerves with either the faradic or galvanic current.

July 10th. Left upper limb. Tactile sensation is lost in the ulnar side of the palm and is felt slightly in the median side of the palm and on the anterior surface of the forearm. It is prompt in the posterior portion of the forearm and is impaired in the outer, posterior, and inner portions of the arm. Motion: the man has partial flexion of the fingers and more in the little and ring fingers; slight motion in the thumb. These movements of flexion of the fingers can be made without first extending the fingers. He has slight flexion of the wrist, more on the ulnar side (action of the flexor carpi ulnaris).

He can flex the forearm upon the arm so as to touch the hand to the face, chiefly by the action of the supinator longus muscle. He can extend the hand on the forearm better than he can perform any

FIG. 8

Photograph taken in December, 1905, showing the voluntary power in flexion of the fingers of the left hand.

FIG. 9

Photograph taken in December, 1905, showing extension of the fingers of the left hand. Extension is greater when more effort is made, as shown in Fig. 10.

other movement. (The musculospiral nerve was not cut transversely.)

Dr. C. S. Potts made an electrical examination November 7, 1905, and his report is as follows:

Right Arm. Deltoid, triceps, extensors of wrist, supinator longus respond well to the faradic current. The biceps responds, but not so well. In the median and ulnar distribution there is no response to the faradic current. AnClC greater than KClC (KClC very weak) marked modal change. The same maintains for the left arm, excepting that the deltoid does not respond as well to the faradic current as the muscle on the right side does. Owing to the corresponding movements of the arms it is practically impossible to pick out the individual muscles with any more accuracy than is stated above.

FIG. 10

Photograph taken in December, 1905, showing still more extension of the fingers of the left hand than is shown in Fig. 9. The index and middle fingers are doubled, as they were not held quietly while the photograph was taken.

REMARKS BY DR. FRAZIER.

The central end of an efferent fibre can make functional connection with the peripheral end of any other efferent fibre of the same class, whatever be the normal actions produced by the two nerve fibres.[1] Such is the physiological law confirmed by repeated investigations first undertaken by Flourens in 1824, upon which is based the principles of the operative treatment of palsies by nerve transplantation.

This principle is applicable to all forms of paralysis—to infantile spinal paralysis, to facial paralysis, to the paralysis due to traumatism of the peripheral nerves. Having proven beyond question of doubt the propriety of practising nerve anastomosis upon selected cases of infantile paralysis, there remains to be considered from the surgeon's point of view the mode of procedure. Several methods

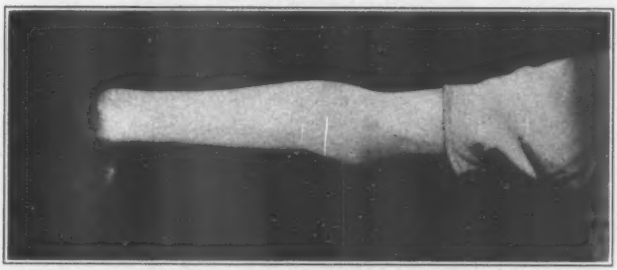
[1] Langley and Anderson. Journal of Physiology, 1904, vol. xxxi.

have been proposed and with each method the results have been variable. Too few cases have as yet been reported to enable one to deduce any conclusions based upon positive clinical data. The advantages which may be claimed for one method or another must be based chiefly upon theoretical grounds. These deal chiefly with the biological problems concerned with the regeneration of nerve fibres. Inasmuch as, at the present time, two so radically different theories as to nerve regeneration are entertained, it is not to be wondered at that different views should be held by surgeons as to the best method of effecting the anastomosis. These are:

1. Lateral anastomosis of the peripheral segment of the nerve to the paralyzed group into the nerve supplying the unaffected group of muscles. (See Fig. 13, No. I.)

On theoretical grounds at least it may be assumed that the best results will follow an end-to-end anastomosis. No matter which theory one accepts, the central or peripheral, the best opportunity

FIG. 11



Photograph taken in December, 1905, showing the ability to raise the right upper limb. The operation on this limb was performed June 13, 1905.

for one set of nerve fibres to unite with another is afforded by bringing into apposition the free ends of one with those of the other. When applied to the treatment of infantile palsy there is a strong objection to this method. We must bear in mind that there has been a certain percentage of failures, and one hesitates therefore to adopt a procedure which may aggravate rather than improve the condition existing prior to operation. Thus for example, if we split off from the unaffected nerve a flap with which to establish an end-to-end anastomosis with the affected nerve, we are robbing the healthy group of muscles of a portion of its nerve supply and may thereby permanently weaken that particular group. Dr. Spiller and I have therefore preferred the lateral anastomosis; that is, implanting the peripheral segment of the affected nerve into the unaffected nerve where the paralysis is not extensive, recognizing and acknowledging the possibility of failure in a certain percentage of cases.

2. End-to-end anastomosis of the peripheral segment of the affected nerve with the central end of a segment split from the unaffected nerve. (See Fig. 13, No. IV.)

Should, however, with the perfection of the technique and with additional clinical experience, it be clearly demonstrated that there is sufficient assurance of restoration of function to the paralyzed muscles to warrant such interference with the nerve supply of the healthy group, this would be the operation of choice, and this or the operation following would probably be necessary where the paralysis is in several muscles.

3. Lateral anastomosis of the central end of a segment, split from the unaffected nerve into the affected nerve (See Fig. 13, No. II.)

My attention was first called to this method of establishing an anastomosis by Hackenbruch.[1] Referring to Fig. 13, Nos. I. and II., it

FIG. 12

Photograph taken in December, 1905, showing the flexion of the right forearm on the arm.

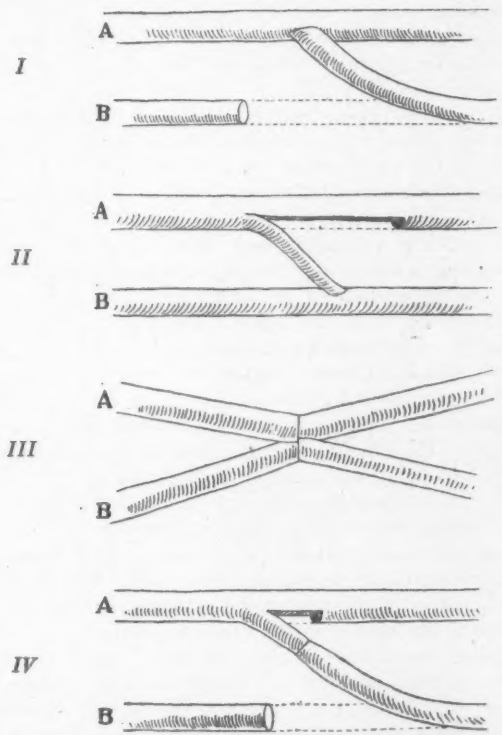
will be seen at once that one method is exactly the reverse of the other. Believing in the central rather than the peripheral theory of regeneration, Hackenbruch thinks this is the more logical mode of procedure. He believes that there would be a very much greater opportunity of functional union between the affected and the unaffected nerves if a flap from the unaffected nerve be engrafted into the affected nerve, since by this plan the young axis cylinders which sprout out from the central stump will almost surely find their way into the fibres of the paralyzed nerve. If, on the other hand, the paralyzed nerve is cut and grafted into the healthy nerve, accepting as he does the central theory of regeneration, he believes it more or less a matter of chance whether the new axis cylinders of the healthy nerve will find their way into the fibres of the paralyzed nerve.

[1] Loc. cit.

4. End-to-end anastomosis of both central and peripheral ends of the affected nerve into the split segments of the unaffected nerve. (See Fig. 13, No. III.)

Dr. Spiller has already referred to Basil Kilvington's investigations. The latter, as a result of his experience with dogs, only recommends an end-to-end anastomosis using both peripheral and central segments of the affected nerves, on the ground that

FIG. 13



Diagrammatic representations of various modes of anastomosis. *A* represents the unaffected, *B* the affected nerve.

there may be a few fibres in the affected nerve which are functionally active and should not therefore be sacrificed. This operation might be applied with reason to those cases in which there is only partial and not complete paralysis in the affected group. The suggestion is not a practical one, however, since one would hesitate to recommend an operation where there was only partial disturbance of function. As to his recommendation that both the affected and

unaffected nerves be divided before the anastomosis is affected, Spiller says this hardly seems a wise procedure. I would go still farther and call it distinctly an unwise procedure.

5. Lateral anastomosis of one or more muscular branches of the affected into the unaffected nerve.

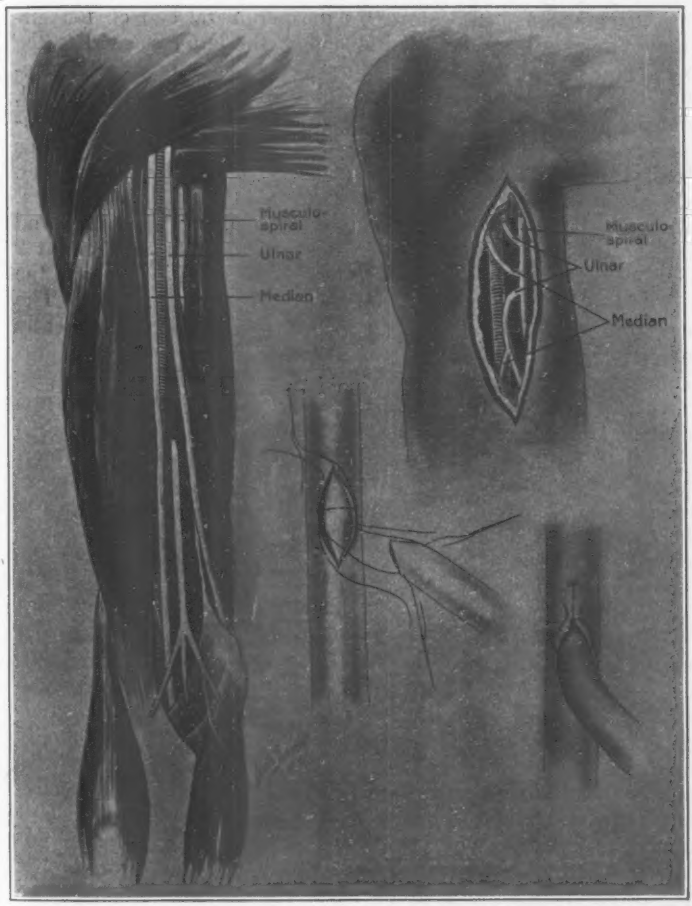
This method is applicable of course to those cases in which but a single muscle is affected. Thus in a patient of Dr. Spiller's (case unpublished) the paralysis was limited to the tibialis anticus. The other muscles of the extensor group were not affected. Under such circumstances it is manifestly unwise to tamper with the nerve supply of the entire group. Accordingly the three minute branches supplying the tibialis anticus were divided and implanted into the musculocutaneous.

Once having determined upon the general plan of procedure, there remains to be considered the details of the technique. These will be taken up in the discussion of the operation for athetosis.

The principles underlying the application of nerve anastomosis in the treatment of athetosis have been referred to by Dr. Spiller. The first operation was performed March 16, 1905. An incision 4½ cm. long was made along the course of the brachial vessels and nerves in the upper half of the left arm. The ulnar nerve was exposed and freed from the areolar tissue throughout the length of the incision. The median nerve was exposed and isolated above the point at which it crosses the brachial artery and the musculospiral nerve for an equal distance. After the introduction of four sutures about 1 cm. apart into the ulnar nerve, two on either side, the nerve was divided between the two sets of sutures and the proximal and distal ends respectively implanted into the musculospiral. Four sutures were introduced in a similar manner into the median nerve, and after the nerve was divided the central end was implanted into the musculospiral nerve and the distal end was implanted into the ulnar nerve. The latter step was adopted because it was feared that too much traumatism might be inflicted upon the musculospiral if each of the four ends of the divided median and ulnar nerves were attached to it. The distal end of the median nerve was attached therefore into the distal segment of the ulnar nerve. The precise manner in which these anastomoses were made is graphically depicted in Fig. 14. At the points of anastomosis the nerves were enveloped with Cargile membrane, the wound closed with interrupted silkworm-gut sutures, and a plaster-of-Paris bandage applied over the dressing, binding the arm to the side. Despite the application of the fixation dressing it was not possible to keep the limb absolutely quiet owing chiefly to the frequent and violent contraction of the biceps muscle, whose nerve supply had not been interfered with. The seat of operation was subjected to so much disturbance through the uncontrollable activity of this muscle that I feared the process of union

and regeneration might be seriously interfered with. Accordingly on April 17th, under my direction, Dr. Van Kaathoven performed upon the same arm a second operation designed to regulate the

FIG. 14



(*a*) To the left a sketch of the normal anatomical relations. (*b*) To the right and above, the manner in which the anastomoses were made in the operation on the left arm. (*c*) To the right and below, the introduction of sutures for a lateral anastomosis, two anchor sutures and a mattress suture.

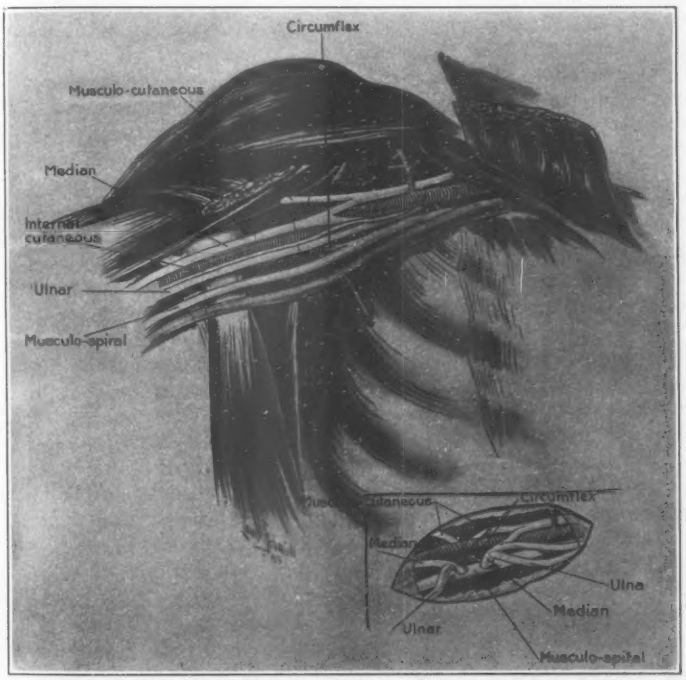
movements of the biceps muscle. An incision about 10 cm. long was made along the line of the axillary vessels and brachial plexus. The pectoralis major muscle was partially divided in order to

afford a freer exposure. The circumflex and musculocutaneous nerves were isolated, their identity tested with an electric current, and two pairs of sutures introduced into each nerve; the nerves were divided between each pair of sutures and an end-to-end anastomosis effected in the following manner: the central end of the musculocutaneous was sutured to the peripheral end of the circumflex nerve, and the central end of the latter sutured to the peripheral end of the former. The nerves at the point of anastomosis were enveloped in Cargile membrane, the wound closed, and the arm bandaged firmly to the side. On June 13, 1905, encouraged by the results of the operation on the left arm, it was decided to carry out very much the same procedure in the right arm. The performance of this operation I entrusted to Dr. Van Kaathoven. An incision about 7 cm. in length was made over the brachial and axillary vessels, dividing the skin, superficial fascia, and about 2 cm. of the pectoralis major muscle. This incision exposed the vessels and brachial plexus. Each nerve was freed in turn. The musculocutaneous and circumflex were divided, and subsequently sutured in the following manner (see Fig. 15): the proximal portion of the circumflex into the distal portion of the musculocutaneous, and the distal portion of the circumflex into the proximal portion of the musculocutaneous. The median and ulnar nerves were then divided and a lateral anastomosis effected between the distal portion of the median and the musculospiral and between the ulnar and median. Similarly on the proximal side the proximal ends of the median and ulnar were united by lateral anastomosis. The muscle wound was closed with a double row of catgut sutures, the skin wound with interrupted silkworm sutures. A piece of rubber tissue, as a drain, was inserted into the apex of the axilla.

TECHNIQUE. Too much stress cannot be laid upon the importance of paying the strictest attention to details in the performance of operations dealing with the cranial or peripheral nerves. The nerves themselves must be subjected to a minimum degree of traumatism, otherwise the process of regeneration will be materially interfered with. To this end the nerves should never be grasped with forceps. In order to avoid the necessity of steadying the nerve while the suture is being introduced, we make it a practice to insert the suture before the nerve has been divided. (See Fig. 16.) If this precaution is taken it will not be necessary at any stage of the operation to grasp the nerve with forceps. When a nerve has to be divided it is very much better to use a sharp knife than a pair of scissors; the latter necessarily pinches and bruises the nerve fibres. It is scarcely necessary to call attention to the impropriety of including in the sutures any portion of the nerve but the sheath. If any nerve fibres are included in the suture these fibres will be so squeezed and crushed when the suture is tied that they will undergo degeneration. Anything which excites the formation of an excess

of cicatricial tissue in or about the site of the anastomosis should be scrupulously avoided. The success of the operation depends: first, upon the nicety with which the apposition is effected and maintained; and secondly, upon the amount of cicatricial tissue at the site of anastomosis. The freer the nerves are at the point of anastomosis from the invasion of scar tissue the better will be the result. Everything which excites the tissues to more or less intense reaction, and therefore to the development of scar tissue, is a menace to the operation. Thus, wound infection is almost invariably fatal

FIG. 15

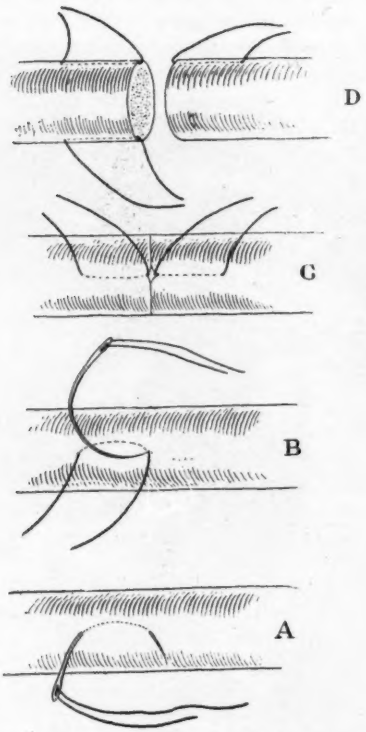


(*a*) Showing normal relations of nerves and vessels. (*b*) To the right and below, a sketch showing the way in which the anastomosis was effected in the operation on the right arm.

to success. The dissection should be as delicate as possible, so that a minimum degree of traumatism be inflicted upon the tissues; the incision should be made preferably to one side or another and not directly over the course of the nerve. The minimum number of sutures should be used, and after the anastomosis has been effected the nerves should be enveloped with Cargile membrane to prevent the invasion of scar tissue. As to the technique to be

observed in the introduction of the sutures, this will depend somewhat upon the way in which the anastomosis is to be made. In an end-to-end anastomosis two or three sutures will suffice to maintain apposition; in a lateral anastomosis the sutures should be introduced in the way illustrated in Fig. 16. Before dividing the nerve two sutures are introduced, one on either side only through the sheath. These sutures, when passed through the sheath on either side of the

FIG. 16



A, *B* and *C*, showing the way in which the sutures are introduced before the nerve is divided *D*, showing the nerve after division with sutures in place.

slit in the undivided nerve, are tied and serve to anchor one nerve to the other. In order to close the slit in the sheath and also to prevent the tip of the nerve from becoming disengaged a third suture is needed. To meet both these indications I have found a modified mattress suture very satisfactory. (See Fig. 15.)

After the dressing is applied the limb should be encased in a plaster cast in order to ensure absolute rest, and I think it advisable

to keep the limb perfectly quiet for four to six weeks. At the end of this period the cast is removed and the patient is then allowed to use the limb. The success of these operations depends in large measure on the faithfulness with which the after-treatment is carried out. Massage, galvanism, and prescribed exercises must be insisted upon and continued for six months to a year—continued as long as the condition is improving.

Results. Whether or not the results of this operation will prove that an equalization of power or force between the two groups of muscles—the flexors and extensors—will be established remains to be seen. It will be interesting to note what influence the innervation of the musculospiral nerve will have upon the muscles supplied by the ulnar and median, and *vice versa*, what influence the innervation of the median and ulnar nerves will have upon the muscles supplied by the musculospiral. What will be the effect upon the extensor group of the transmission of the stronger impulses from the central segment of the median and ulnar nerves into the musculospiral nerve? Will these same impulses be diverted again from the musculospiral nerve into the peripheral segments of the median and ulnar nerves, or will there be no direct communication between the fibres of the proximal segments of the median and ulnar nerve with those of the distal segments? What would be the effect of stimulating electrically the central segment of the median or ulnar nerves? Would we get response in the distribution of the musculospiral nerve alone or in the median and ulnar nerves too? These are some of the interesting questions that suggest themselves, and no doubt a number of instructive phenomena concerning the transmission of nerve impulses and nerve regeneration may be observed in the case upon which we have operated. That one nerve can perform the function of another when both are physiologically united is a matter of common knowledge. Thus, for example, in cases of facial palsy we know that after anastomosis of the facial nerve to the hypoglossal or spinal accessory nerve either of these nerves may transmit impulses directly to the muscles supplied by the facial nerve, as well as to those muscles over which they originally presided. That the cortical centres of one nerve may be educated to preside over those of one or more is also an accepted phenomenon. Taking these physiological laws into consideration, it has occurred to me that in case the present plan of anastomosis which we have adopted in the treatment of athetoid movements is not successful, we might go even further than Dr. Spiller has suggested. Thus, for example, we might cut off entirely the connection of the nerve supply of the flexor group by permanently disconnecting the central segments of the median and ulnar and relying entirely upon the musculospiral nerve innervating the flexor group through its anastomotic connection with the distal segments of the median and ulnar nerves.

As to the results which have actually been obtained in the patient upon whom we have operated, we are able to make a favorable preliminary report. After recovering from the paralysis immediately following the operation the patient is regaining power in the distribution of the flexor group, and, as will be seen in Figs. 4, 5, 6, and 7, he is now able in the left extremity to voluntarily flex the fingers, the wrist on the forearm, and the forearm on the arm. At the last examination, November 6, 1905, the following notes were made by Dr. Spiller:

Left Upper Limb. There is still some stiffness of the entire limb, but this is not always present. The limb jerks very little when the man wishes to hold it quietly, and is not excited, but sometimes there is slight jerking on voluntary movement. When the left hand rests on some support he can almost fully extend the first finger and can extend the other fingers partially. He can partially flex all the fingers and can flex the wrist almost to a right angle, the power being greater on the ulnar side. He can flex the forearm on the arm to about the normal extent, and can partially raise the arm at the shoulder. Sensations for touch and pain are normal in all parts of the left upper limb, except in the palm of the hand, where there is still much impairment in the ulnar distribution. He cannot approach the thumb to the little finger. Muscular atrophy is slight.

Right Upper Limb. He still has athetoid movements at the shoulder, but they are apparently entirely or nearly entirely in the latissimus dorsi and muscles over the scapula, as the arm is drawn downward and backward during the spasmodic movements. He has slight return of power in the flexors of the fingers, but has much power in the extensors of the wrist. He can flex the forearm to a right angle with the arm and elevate the arm to a right angle with the trunk. He has much less involuntary jerkings at the right shoulder when he is not excited. Sensations for touch and pain are normal in the limb, except over the anterior aspect of the forearm and in the ulnar and median distributions of the hand.

There is therefore partial flexion and extension of the fingers of the left hand, much power in flexion and extension of the left hand on the forearm, and of the left forearm on the arm, and in elevation of the left arm at the shoulder. These movements are made with difficulty.

The return of power in the right upper limb is not yet so good as in the left, but this is because the operation on the right limb was performed more recently. The athetoid movements at the shoulder are in muscles that have not been operated upon. The voluntary movement present in the right limb is shown by slight flexion of the fingers, extension of the hand on the forearm, flexion and extension of the forearm on the arm, and elevation of the arm at the shoulder.

The electric reactions are reported in the case history.

THE FUNCTION OF THE LEFT PREFRONTAL LOBE.

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In a monograph published in 1894[1] I first suggested a more limited seat of control for the intellectual faculties than seems to have been suspected by previous writers; and in a systematic study of intracranial injuries subsequently published[2] I arrived, by comparison of symptoms with postmortem findings in a large number of cases, at a tentative conclusion that this control resided exclusively in the left frontal lobe. Two years later,[3] having observed an additional number of cases which confirmed the correctness of my original conclusion, I collated the entire series, together with such other analogous cases as were available, in an article which summarized the facts and inferences upon which that conclusion was founded. The evidence adduced seemed to me to then justify three final propositions which might be considered established. These were:

"First. The more absolutely the lesion is limited to the left prefrontal lobe, the more positive and distinctive are the symptoms of mental default.

"Second. The integrity of the mental faculties remains unimpaired with right frontal lesion, even though it involves the destruction of the entire lobe, or even extends to the entire (right) hemisphere.

"Third. The exceptional instances in which seemingly opposite conditions exist are always reconcilable, on more careful examination with the assertion of an exclusive control of the mental faculties residing in the prefrontal region of the left side."

To which was added: "If, then, the same nature and degree of proof, which is deemed sufficient for the localization of other cerebral functions, may be accepted in case of the mental faculties their centre of control has been established."

In the interval since this later publication I have noted and recorded a still further number of cases of cerebral injury in which the distinctive lesion was found to be frontal, and in which the same relation of lesion to symptoms existed. These cases, while in no way more convincing than those which have preceded them, serve, as the result of additional experience, to strengthen conclusions perhaps already sufficiently well founded. They are eleven in number: three in which the lesion was limited to the left lobe; three in which

[1] New York Medical Journal, November 10, 1894, to January 12, 1895.
[2] Traumatic Injuries of the Brain, D. Appleton & Co., New York, 1897.
[3] The American Journal of the Medical Sciences, April–May, 1902.

the right lobe was also implicated, but in lesser degree; and five in which the lesion was limited to the right lobe.

Their histories are presented in brief. As in previous series, cases characterized by primary and permanent unconsciousness, or by practically uninterrupted delirium, or in which death was almost immediate, have not been included.

CASE I. *Left Frontal Lobe.*—A man from thirty to thirty-five years of age, who some ten years before had received an injury of the head was admitted to Bellevue Hospital immediately after the infliction of another injury of that part. No further history was obtainable. On admission he was conscious, but dull and apathetic, taking no notice of his surroundings; pupils normal; no hemorrhages; no loss of rectal or vesical control; temperature 100°; pulse 120; respiration normal; radial pulsations symmetrical at the two wrists; lacerated wound four inches long in right parietal region and an incised wound just behind left malar process; right eye nearly closed by ecchymosis, with a subconjunctival hemorrhage confined to its external aspect; face drawn to left side; wrist-drop, which was afterward learned to be a chronic condition; no other paralysis; right patellar reflex increased; left diminished.

Second day: general condition unchanged; temperature, 101°; pulse, 120; respiration, 30.

Third day: answered questions rather more intelligently and spoke more distinctly; temperature, 101.8°; pulse, 120; respiration, 30.

Fourth day: patient very dull and apathetic; did not answer questions readily nor comprehend accurately; loss of rectal and vesical control; temperature, 102°; pulse, 100; respiration, 30.

Fifth day: patient still apathetic; mumbled; cried when questioned; temperature, 101°; pulse, 96; respiration, 24.

Sixth day: patient weaker and much of the time delirious; temperature, 101.5°; pulse, 100; respiration, 24.

Seventh day: patient restless and delirious; temperature, 103°; pulse, 128; respiration, 32.

Eighth day: patient in stupor; died at night. Temperature, 106.8°; pulse, 180; respiration, 48.

Necropsy. (Examination of brain by Dr. Harlow Brooks.) "The brain, as a whole, is somewhat longer, firmer, and narrower than usual, and the left occipital lobe shows an abnormal groove on the left posterior border. The markings are fairly typical. The meninges are generally thickened over the entire brain.

"The right hemisphere throughout shows no gross lesions of note.

"On the left side there is a recent hemorrhagic softening, apparently following laceration just posterior to the ascending limb of the fissure of Sylvius. At the posterior extremity of the horizontal limb of the same (left) fissure there is found a shrunken, depressed pit 3.1 cm. in depth by 1.4 cm. in breadth extending into the cerebral substance to within 5 mm. of the roof of the lateral ventricle. The

tissues surrounding this cyst are sclerosed and the convolutions are retracted and atrophic. A sclerosis is evident even in the occipital lobe.

"The left frontal lobe is considerably smaller than the right, the measurements at the level of the fissure of Sylvius being 15 cm. for the left and 15.5 cm. for the right. The convolutions of the left frontal lobe are generally atrophic, while those of the right of the same configuration are large and of normal appearance. Section of the left frontal lobe shows an extreme degree of general sclerosis.

"The bloodvessels at the base are markedly arteriosclerotic."

CASE II. *Left Frontal Lobe.*—A man aged fifty-three years fell down a flight of stairs, and next day went to the police station to complain that he had hurt his head. He then answered all questions readily, but in a few moments could not connect words to form sentences. On arrival of the ambulance, though his speech was confined to disconnected words, he could gesticulate and could comprehend whatever was said to him. His facial expression was intelligent and he could read and write. His temperature was 98.8°; his pulse 132, and his respiration 30, and somewhat labored and noisy. His face was flushed, skin dry and warm, mouth dry and parched, and pulse normal, except that the left was a little fuller than right. There was no paralysis and no loss of rectal or vesical control. A contusion extended from the right parietal eminence to the inferior occipital curved line and as far outward as the border of the mastoid process, with ecchymosis of the mastoid tip. On the second day he was restless and still unable to speak. His pupils were contracted and without reaction to light. Temperature was nearly normal; pulse and respiration were somewhat increased in frequency. A slight hemorrhage from the right ear, which had existed since his admission, ceased during the afternoon. During the three following days the mastoid ecchymosis increased; the pupils were contracted, but reacted to light; vesical and rectal control were successively lost; temperature varied from 98° to 100.8° each day until the last, when it rose to 102°; pulse ranged irregularly from 80 to 124, and respiration from 18 to 30. Muscular disorders were prominent symptoms; paroxysms of clonic spasms of the face and lower jaw on the first day increased in frequency and duration, and on the second were followed by prolonged tonic general convulsions and by paralysis of the right arm and leg and left face. On the third day muscular spasms of the face and extremities were less violent and the paroxysms shorter and intervals longer. Blood pressure which on the second day was 170 mm. fell on the third to 143 mm. The patient at this time was trephined: first, under the hæmatoma above and behind the right ear, and, afterward, over the left arm centre, and in each instance the dura mater was incised without disclosing any lesion. The patient died thirty-six hours later, without special change in symptoms. It was said by the

attendant that up to the morning of his death he seemed to comprehend what was said to him.

Necropsy. (Made by Dr. Harlow Brooks.) "Fissure extending from the right greater wing of sphenoid, along posterior border of petrous portion of right temporal to posterior inferior angle of right parietal bone; no epidural hemorrhage; pia mater excessively congested, universally thickened, and slightly adherent on the left side; subarachnoid hæmatoma forming a bulging oval mass, 7 cm. in its greatest width, originating from left Sylvian artery, which was partly filled by thrombosis, and extending along Sylvian to median fissure; subjacent cortex considerably eroded. This hæmatoma was situated between the vertical and horizontal arms of the Sylvian fissure, and encroached upon the left frontal lobe only at the base of the third convolution, which was later found to be the seat of hemorrhagic softening. Small vessels containing coagula were found throughout the left hemisphere. The bloodvessels at the base were moderately thickened; ventricles normal except for a slight congestion."

This case is especially interesting as one of the few with a fatal termination in which aphasia is unaccompanied by obvious mental impairment. Many such patients recover, and of the few who die primary and permanent delirium or unconsciousness usually mask all other mental indications. In this instance, following the occurrence of aphasia, the patient in the absence of alexia or agraphia could indicate an apparently normal mental condition, and even up to the day of his death was able to manifest at least a comprehension of all that was said to him. This case is confirmatory of previous observations that lesions confined to the posterior part of the left frontal lobe do not impair the action of the intellectual faculties, except so far as aphasia itself may be considered an intellectual rather than a simple motor defect.

Case III. *Left Frontal Lobe.*—The patient, a man aged thirty-five years, fell thirty feet and was primarily unconscious. On immediate admission to the hospital his temperature was 98.8°, pulse 88, and respiration 20; his pupils were normal. He was drowsy and his cerebration slow. He had a lacerated wound over the right parietal eminence extending to the periosteum and no apparent fracture. There were no external hemorrhages. There was no loss of rectal or vesical control and the urine was normal. On the third day there was a sudden rise of temperature to 105°, while the pulse and respiration remained normal—78 and 20. The patient was stupid or apathetic, but could be aroused to answer questions after some interval. The white blood count was 14,000. The wound was found to be aseptic, and there was no pulmonary complication. On the fourth day the patient was unconscious, with temperature 106°, pulse 100, and respiration 36. On the fifth and sixth days the range of temperature was from 105° to 103.6°,

and of pulse from 120 to 130, and vesical control was lost. From the seventh to the tenth day the range of temperature, pulse, and respiration was not materially changed, and the patient could be aroused from his stupor. From the tenth to the seventeenth days his pulse remained frequent and his temperature high. On the last of these days his temperature fell to 101,° his pulse to 96, and his respiration to 24 to 28, and his comprehension was rather less delayed. On the eighteenth day he again became unconscious, with lack of both rectal and vesical control; and on the nineteenth day he died.

Necropsy. No cranial fracture; no meningeal hemorrhage or inflammation; blood clot occupying whole central portion of left frontal lobe, and hemorrhage from this point extending into lateral ventricles; moderate general cerebral hyperæmia.

In this case a moderate general contusion was evidently followed on the third day by a hemorrhagic destruction of the whole central portion of the left frontal lobe, as indicated by the sudden great rise of temperature with normal pulse and respiration, and with immediate stupor and delayed and limited comprehension.

CASE IV. *Both Frontal Lobes.*—A man aged forty-seven years fell twelve feet and struck his head upon a hydrant. He was said to have been primarily unconscious and to have bled profusely from a wound of the scalp. On immediate admission to the hospital he was still unconscious: temperature, 102°; pulse, 150; and respiration 28; pupils immovable and unequally dilated; blood pressure in right and left radial arteries 90 and 87 mm.; scalp wound in left posterior parietal and in left occipital region, the first of which bled profusely, and the second of which disclosed a fissure extending downward and outward toward the cranial base; no paralysis or anæsthesia; reflexes exaggerated; retention of urine and loss of rectal control. For the twelve days following he was constantly delirious, usually noisy and restless, occasionally quiet and stupid. His pupils were sometimes normal, sometimes unequally dilated; vesical control was sometimes lost, and sometimes catheterism was required; blood pressure rose to 144 mm. in the right and to 130 mm. in the left radial artery, and later fell to 110 mm. in each; temperature only once exceeded 99°; pulse ranged from 100 to 110, and respiration from 22 to 24. For the next six days his condition remained without material change. He was usually actively delirious at night, requiring mechanical restraint, and was quiet, stupid, and sleeping much by day. When his condition rendered examination practicable it was difficult or impossible to fix his attention. If he began to speak with some distinctness so that a few words could be understood his speech soon became a mere mumbling or an unmeaning jargon. His articulation when his words were intelligible was normal and he was apparently not aphasic. He never recognized his wife and only once a friend.

He could tell his name, but could answer rationally no other question. He evidently thought he was at home, but nothing else could be gathered from his mumblings and incoherent speech. At the end of this time an ophthalmic examination, made by Dr. P. A. Callan, showed an early stage of descending optic neuritis. Until the last two days temperature, pulse, and respiration were practically normal. On the fifth day of this period temperature rose from 99° to 104.2°, pulse from 92 to 130, and respiration from 26 to 28. On the sixth and seventh days pulse and temperature continued high, and he was transferred to Bellevue Hospital.

On admission there he would answer only an occasional question; both pupils dilated and reacted sluggishly to light and accommodation; tongue dry and brown and teeth covered with sordes; left arm rigid; no areas of anæsthesia; patellar reflexes delayed and diminished; wounds of scalp yet unhealed. Temperature, 102.4°; pulse, 112; respiration, 24; radial pulsations of moderate tension.

The patient died twelve days later—thirty-one days after receipt of the injury. Up to the time he became comatose, two days before his death, he continued to be noisy at night and quiet by day. He would sometimes answer simple questions, was sometimes angry and abusive, and was habitually mumbling to himself, rambling, and incoherent. His temperature ranged from 99° to 100.5°, until a final rise to 103.°

Necropsy. (Made by Dr. Harlow Brooks.) Linear fracture of occipital bone on the left side extending around into foramen magnum, and by a secondary fissure nearly separating the left petrous from the squamous portion of the temporal bone, and also divulsing sections of left temporal and parietal articulations; extensive pachymeningitis externa originating from site of occipital fracture and extending forward to left temporal fossa; typical pachymeningitis interna diffusa and a slightly suppurative arachnitis, with large amount of turbid serous fluid at the base of the brain; extensive pus formation involving left temporal and anterior portion of left occipital lobe; abscess cavity 2 cm. in diameter in posterior portion of left cerebellar lobe; consistency of the brain generally increased; atrophy of both frontal lobes, more marked in the left; measurements taken at level of Sylvian fissure: right frontal, 15.6 cm.; left frontal, 13.7 cm.; complete thrombosis of left lateral sinus; internal left ear widely opened by fracture, and dural membrane greatly inflamed.

CASE V. *Both Frontal Lobes.*—A man about about forty years of age, who had been found unconscious in the street and whose previous history was unknown, was admitted to the prison ward of Bellevue Hospital. On admission he was still unconscious; temperature 100.2°; facies dazed and pained; slight œdema and ecchymosis over right mastoid process; ecchymosis encircling the right eye, with some extravasation of blood beneath the conjunctiva and

slight exophthalmos; both pupils normal in reaction; right pupil slightly dilated; neck rigid, muscles generally spastic; plantar and patellar reflexes slightly increased; no external hemorrhages; no areas of anæsthesia; no rectal or vesical control. Two hours after admission he had one general convulsion.

Second day: patient restless, throwing his hands and arms about and often yawning, muttering incoherently, rolling his eyes, and at intervals fixing them upon the ceiling with a vacant look.

Third day: patient's attention could be attracted, and he tried ineffectually to reply when questioned, but could make only a mumbling noise; right pupil still the larger; muscles still spastic, most markedly in the upper extremities; fingers, wrists, and elbows flexed.

Fourth day: aphasia; dilatation of right pupil; lack of rectal and vesical control still continued.

Fifth day: ecchymosis behind the right ear increased; patient could only occasionally comprehend and reply in monosyllables to questions.

Sixth day: condition unchanged. When asked to squeeze the hand of the examiner the patient did so finally after many requests and much delay. On the previous day, though his attention was engaged, he seemed unable to comprehend this request, or another, that he should show his tongue, even when both requests were re-enforced by example; neither one elicited any response.

Seventh day: patient answered every question with the one response, "yes," and seemed quite satisfied with his reply. He did not recognize familiar objects—as key, knife, etc., and replied with "yes" when asked their names. He insisted that his name was Jenkins, and not Brown, as it really was. He had little power in his hands at any time and moved them feebly and aimlessly about.

Eighth day: he continued to answer "yes" to all questions, and, when given pencil and paper, wrote a number of disconnected words—*e. g.*, "Hotell"-Doting-Homes"—the last repeated; the letters well formed. His pulse became weaker.

Ninth day: he became unconscious in the early morning and died in the afternoon, the muscles of the arms, which were previously relaxed, having become spastic and the reflexes increased. The right pupil was contracted, the left dilated, and the skin was sensitive. The temperature on the second day rose to 102°, and the third fell to 101°, on the fourth to 100°, and thereafter was stationary at 99°, until after the occurrence of unconsciousness, when it rose to 102.4°. The pulse on the second day rose to 120, and thereafter ranged from 78 to 92, until the end, when it fell to 60. Respiration was always normal.

Necropsy. Contusion of right temporal muscle; linear fracture of right parietal bone extending from anterior inferior angle upward

and backward for a distance of two inches; oval epidural clot directly beneath the parietal fissure, two and one-half inches long, one inch wide, and one-quarter inch thick, with the underlying convolutions flattened and depressed. There was a second epidural hemorrhage, with the blood still fluid over first and second right temporal convolutions.

Further examination by Dr. Harlow Brooks. "Numerous petechial extravasations into pia mater over right frontal lobe, especially on the inferior aspect. These are accompanied by small hemorrhages into the substance of the adjacent cortex, causing areas of softening of greater or less extent; the largest being found: one on the inferior surface, 1 cm. from the median line of the anterior border, and another just below the ascending branch of the Sylvian fissure. Numerous smaller hemorrhages are found scattered throughout the cortex, the greater part of which evidently originated from the vessels of the pia mater. On the left side of the brain meningeal extravasation covers the entire surface of the frontal lobe, with extensive laceration of the inferior aspect of that lobe and of the tip of the temporal. The Island of Reil is completely destroyed. The cerebral vessels show marked sclerosis. Section of the brain shows a general hyperæmia, and hemorrhages of considerable size in all parts of the pons. There is also an area of softening extending from the Sylvian artery into the substance of the left hemisphere as far as the posterior commissure. The laceration of the left temporal lobe destroyed its anterior two-thirds and extended into the left hemisphere without compressing or involving the internal capsule. The inferior portions of the first, second, and third left frontal convolutions were softened and infiltrated with blood."

The following case was cited in the writer's original series of 300 "Condensed Histories of Cerebral Traumatisms" (1897), but was not included in either of the previous series of frontal lesions.

CASE VI. *Both Frontal Lobes.*—A young man in a collision was thrown from his bicycle and was primarily unconscious. He was taken to his house, where he had a convulsion, and was then removed to a hospital, where he remained forty days. No record of his condition during this time is obtainable. He was afterward treated by an oculist for exophthalmos. He resumed his occupation and was said to have been in good physical health, but a distinct mental change was observed by his family. His temper was irritable and his conversation, which had been hitherto irreproachable, became remarkably obscene, without apparent appreciation on his part of its impropriety. One week before his admission to St. Vincent's Hospital, and six months after the reception of the injury, he became suddenly apathetic and soon fell into a stupor, with loss of fecal and urinary control and the accession of a febrile movement. When admitted to the hospital he lay motionless without indication

of intelligence. During the five days he survived he was afterward continuously delirious. Ophthalmic examination disclosed exophthalmos of the right eye, with descending optic neuritis, and increased tension and œdema of the retinoid area (Callan). Temperature progressively increased to 106° and pulse rate to 146.

Necropsy. The line of a consolidated fracture extended from the left temporal fossa across the forehead three-fourths of an inch above the supraorbital ridges. The inner half of the left orbital plate, and the left lesser wing of the sphenoid bone had disappeared. The horizontal plate of the ethmoid and superior surface of the sphenoid body had also been destroyed; the exposed cellular spaces below were blackened and infiltrated with pus. A cyst projecting from the right frontal lobe rested in this central cavity of bone. Both frontal lobes were much softened, yellowish in color, and adherent to the dura mater. The anterior inferior portion of these lobes was too much softened for examination; their superior surfaces were of normal character. The cyst contained from three to four ounces of greenish-yellow pus. There was no evidence of former hemorrhages and no general hyperæmia, but a very œdematous condition of the whole brain substance.

Case VII. *Right Frontal Lobe.*—A man aged thirty-six years was struck, three hours previous to admission, by a large fragment of a bursting emery wheel and was made primarily unconscious. He walked from Newark to New York, several miles, and was then brought to St. Vincent's Hospital by ambulance. He was weak and somewhat apathetic; temperature 100.6°; both eyes contused, pupils normal; no external hemorrhages; compound fracture of frontal bone above the right eye, involving the orbital plate.

Second day: two pieces of bone removed from the orbit, one 2x2 inches and one 1x1 inch in measurement, with several smaller fragments; destruction of anterior extremity of first, second, and third frontal convolutions, altogether forming a cavity about the size of a pigeon's egg.

Seventh day: no symptoms since admission, mental or otherwise; temperature 99° to 101.8°.

Tenth day: complained of malaise; pain in the back of the head; no deliriuin; temperature for three days previous 99.8°, 102°, and 100°; pulse, 58 to 64; respiration, 18 to 20.

Eleventh to twentieth days: no symptoms of importance; drowsiness, restlessness, nervousness, and varied pains at various times; temperature, pulse, and respiration normal.

Fiftieth day: ophthalmic examination by Dr. Callan disclosed descending optic neuritis in the right eye, with scar running through the ciliary body; lesser degree of neuritis in the left eye.

The patient left the hospital four days later without having at any time manifested any indication of mental impairment.

CASE VIII. *Right Frontal Lobe.*—A man aged forty years was shot in the head, and, by way of another institution, a police court, and the House of Detention for Witnesses, was finally admitted to Bellevue Hospital. He was then in a condition of stupor, with paralysis of the left arm and anæsthesia of the left side of the body. The wound of entrance in the right temporal region was without superficial burn or powder mark, and the bullet track passed downward and backward. Temperature 102.8°; pulse, 80; respiration, 28.

Careful measurement showed the bullet to have passed through the central portion of the second right frontal convolution.

Immediate Operation. Comminuted fracture one inch in diameter, with a fragment of bullet removed; osseous wound enlarged by small posterior trephination, and intervening bridge of bone sawed away, exposing a flattened piece of lead; remainder of bullet felt in right posterior occipital region near the cranial base. Two days later there was incomplete facial paralysis, and a little later still the left arm became anæsthetic. The recovery of the patient was rapid. Muscular power was recovered in individual groups of muscles independently of each other; sensation was restored after some fluctuations in its manifestations. There was no mental disorder or default at any time after emergence from primary stupor. At the time of the patient's discharge from the hospital, on the twenty-first day, some deviation of the tongue, when protruded, was the only remaining symptom.

The following case was transferred to my service in Bellevue Hospital by Dr. C. L. Dana, and was operated upon by my then assistant, the late Dr. John A Conway. Dr. Dana subsequently presented the patient to the New York Neurological Society April 2, 1895, but without reference to his mental condition.

CASE IX. *Right Frontal Lobe.*—A young man aged twenty-seven years received a blow upon the left side of the head, which was followed by primary unconsciousness, but by no immediate subsequent symptoms of importance. Three years later he became the subject of general epileptic convulsions. At a still later period he came under the observation of Dr. Dana, and then suffered from a left hemiplegia, with various anæsthesias, intense headache, and double optic neuritis. There had been and were then no indications of mental disorder. On operation a subdural tumor, which afterward proved to be a spindle-cell sarcoma, was discovered which was separable from the brain in the parietal region, but infiltrated the cortex of the whole right frontal lobe upon its superior surface, and anteriorly and laterally extended toward the base beyond the reach of the operator. The patient recovered from the effects of the operation, and a year later had continued to improve in his general condition, and was still free from mental disturbance.

Another case of extensive right frontal lesion without mental

impairment reported by Noyes,[1] but which escaped notice in previous series of cases, may be briefly summarized. It resembles the "Crowbar Case" of Harlow[2] in the nature and extent of the injury, but differs radically in its location and results.

CASE X. *Right Frontal Lobe.*—A young man while shooting was wounded by the explosion of his gun. A piece of iron $4\frac{7}{16}$ inches long, $\frac{1}{2}$ inch wide, and weighing 2 ounces, 5 drams, 25 grains, was driven through the nose and orbit into the cranial cavity and right frontal lobe. He was unconscious four days and "afterward did not lose his mind nor have any delirium." Nearly two months afterward it was noted that "his intelligence was unimpaired," and at the end of five months Dr. Noyes removed the missile from the cavities and cerebral substance in which it had been lodged, and again mentions that "his intellect was clear and his memory unimpaired." This operation was followed by cerebral abscess, trephining for its evacuation, and death after sixteen days, and on the thirty-ninth day after the primary interference. Dr. Noyes states that he continued to be "perfectly intelligent up to within two hours of the end."

Necropsy. The second and third right frontal convolutions were destroyed, and the whole orbital surface of the lobe nearly so; the left frontal lobe was normal.

CASE XI.—This, the final case of right frontal lesion, was seen by the writer through the courtesy of Dr. W. G. Macdonald, of Albany. The patient, then about ten years of age, was operated upon by Dr. Macdonald six years ago for caries of the right frontal and temporal bones, and a large portion of each removed. Epilepsy followed some months later, which has since continued. Two months ago he developed the status epilepticus. He was again operated upon by Dr. Macdonald, who evacuated a large collection of cerebrospinal fluid containing pus which excavated the entire right frontal lobe and extended into the right lateral ventricle. I am informed by Dr. Macdonald that his mental condition has been at all times normal, as it is at the present time. He is coherent, rational, and without delusions. His memory is good and his power of concentration and of comprehension retained.

Cases which terminate in recovery cannot be cited in evidence in the present study of localization, as their symptoms, though characteristic, cannot be verified. Exceptions, of course, must be made of cases in which the frontal lobe has been exposed by operation or compound fracture. The number of recovering cases is much greater than that of cases which terminate in death. This comparatively greater frequency and lesser mortality is but the partial expression of the wider fact that injuries in general of the

[1] A Case of Lodgement of a Foreign Body in the Nose, Orbit, and Cranium, etc., THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, July, 1882.

[2] See Localization of Mental Faculties, etc., ibid., April–May, 1892, p. 29.

anterior part of the brain are more frequent and less fatal than those of its posterior regions; and when the lesion is practically limited to one or both of the frontal lobes, with its consequently localizing symptoms most distinct, recovery is the rule rather than the exception.

The following cases out of many have been selected for transcript as fairly representative of the class to which they belong. The patient when discharged from the hospital has usually exhibited some degree of mental decadence, but not infrequently a normal mental condition has been re-established; a maniacal outcome has been exceptional. The ultimate result is, of course, difficult to ascertain.

CASE A.—A man aged fifty-five years fell twenty feet from a ladder to the ground. He was unconscious for fifteen minutes and was then brought to the hospital. On admission he was conscious, but mentally confused and answered questions slowly. Temperature, 101.4°; pulse, 88; respiration, 24; no external hemorrhages; no muscular disorders; pupils normal; pulse regular; arteries thickened, with a systolic murmur at the cardiac apex.

Second day, A.M.: ten hours after admission patient became again unconscious; left pupil dilated and fixed; surface of body cool; mucous surfaces cyanotic; slight twitching of right arm and face; sensation slightly diminished. Temperature rose to 102°, pulse to 126, and respiration to 40. Later in the day general convulsions occurred and continued for several hours.

Third day: patient still unconscious; temperature 99.2°, pulse 88, and respiration 26; paralysis of right arm and face, with diminished power and sensation in right lower extremity; left pupil unchanged; no vesical control.

Fifth day: patient still unconscious; temperature 103°, pulse 80, and respiration 24; sensation restored in right upper and lower extremities.

Sixth day: patient delirious and noisy; free movements of right arm and leg; continued slight right facial paralysis; left pupil still slightly larger than the right and sluggish in reaction.

Seventh day: patient could answer "yes" and "no."

Eleventh day: answered "yes" or "no" to all questions and was evidently aphasic. Temperature had remained 101°.

Twelfth day: patient actively delirious; temperature, 103.8°; pulse, 110.

Thirteenth day: patient apparently had some power of comprehension, and could repeat words which he heard; patellar and elbow reflexes absent on right side; temperature 101.8°.

Fourteenth day: patient actively delirious.

Sixteenth to twenty-fourth days: temperature, pulse, and respiration normal; patient quiet and aphasic; mental condition difficult to determine.

Transferred to Bellevue Hospital. On admission there he muttered incoherently, and, when spoken to, would pause, look around for the speaker without apparent sense of direction, and then resume his muttering. He would not answer simple questions, though occasionally a few words arranged without reference to meaning could be recognized. Some slight effort at mental concentration when spoken to was also occasionally manifest. During the four days following he was delirious much of the time, but with quiet intervals. Temperature, pulse, and respiration were normal.

He would sometimes answer questions, *e. g.:*

Q. "How long have you been sick?"

Ans. "I tumbled over a fiddle."

Q. "How old are you?"

Ans. "I'm fifty-five; my mother is fifteen."

Q. "What's the matter with you?"

Ans. "I've got three lungs."

Q. "Where did you get them?"

Ans. "A man gave them to me. I don't want them."

At this time, under a misapprehension, he was transferred to the Psychopathic Ward, and thence to the City Asylum. While in the Psychopathic Ward notes were made as follows:

"Sits idly about;" "takes no interest in his surroundings;" "sleeps well; very much confused and contradicts himself continually." At one time says he is very sick "because this is a cross country," and immediately afterward that there is nothing the matter with him, "only this foot," and at another time that it is his stomach, etc.

"Patient much confused; wanders aimlessly about; takes little interest in his surroundings."

"Feeble ataxic movements; straddling gait; deep reflexes exaggerated."

"It is almost impossible to attract his attention; answers at random; makes irrelevant remarks; mind is too feeble to give a clear history; laughs in a silly way."

Two weeks later he was returned to Bellevue Hospital without material change in his mental condition. During the two months following no considerable mental improvement was manifest. He regained rectal and vesical control and became able to walk about the ward, but his gait was ataxic and his reflexes were disordered. He at times answered questions promptly and correctly, could properly designate articles shown to him, and could tell his own name; oftener he was unable to name the most familiar objects about him, to remember his family relations, to appreciate his immediate surroundings, or to reply rationally to the most simple questions. He would insist that his dead wife was living, that his sons were his daughters, that he was two years old, and that the hospital was North Moore Street, or that he had a headache in his groin.

The result of an examination made four months later showed that his general health was good, that he had gained weight, that he had perfect rectal and vesical control, that his pupils were normal, that he had no muscular impairment, that the patellar reflexes were normal, and that he was often rational and coherent. He still had, however, marked motor aphasia, with alexia and agraphia, and his memory was very deficient. He was consequently very uncertain as to his family relationships and personal history.

At the end of another month he was discharged from the hospital with some apparent improvement in his mental condition.

CASE B.—A man, aged twenty-seven years, was said to have fallen down stairs. On admission to the hospital he was still unconscious: temperature, 98°; pulse, 90; respiration, 30; breathing stertorous; right pupil slightly dilated; thin hæmatoma over right eye; no orbital contusion; hemorrhage from the nose. One hour later, marked right orbital ecchymosis, and a little later still extreme conjunctival chemosis. Two hours and a half after admission with temperature and pulse unchanged, respiration increased in frequency to 44 in the minute; four hours later still, temperature had risen to 102°, pulse to 100, and respiration to 40 in the minute. Consciousness was regained during the night. During the three days following respiration varied in frequency from 50 to 62 in the minute, and did not fall below 30 until ten days later. Temperature for thirteen days ranged from 104° to 99.8°, and pulse from 126 to 80. Stertor ceased on the third day, but respiration continued to be laborious and shallow for some time longer. Pulsations in the radial arteries were asymmetrical until the end of the first week. There was no rectal or vesical control until the fifth day, and after that time it was lost by night, though retained by day. There was no paralysis, but some weakness of the muscles of the right face and extremities during the first week. The hæmatoma, ecchymosis, and subconjunctival hemorrhages slowly disappeared. There were no further general physical symptoms, and rectal and vesical control were permanently regained in the third week.

A mental disorder was manifest from the second or third day, when it was noted that though he answered simple questions with apparent comprehension, it was about the extent of his intelligence. On the fifth day he conversed rationally, but on the sixth and seventh his attention was not readily fixed, and he was talkative and incoherent. From the eighth to the twelfth days he answered questions intelligently and coherently, but then, as at all times after he recovered consciousness, he believed himself to be still in the hotel where he was employed at the time he received his injury, and still engaged in running an elevator, going out and coming in, and doing all the things which he was there accustomed to do. From the thirteenth to the sixteenth days his mental condition somewhat deteriorated. He was still coherent, his attention could be readily

fixed, and he answered all questions with propriety; but his delusions increased in number and were constant. He had no recollection of anything which had occurred after his accident, and no conception of his surroundings. A few days later he thought he was in a hotel at Greenwood (Cemetery), and when told that he was in a hospital seriously thought it was about the same thing.

At the end of the fourth week he no longer had delusions, and his mental condition was normal.

CASE C.—A lad aged eleven years was found unconscious by the ambulance surgeon, with no previous history obtainable. On admission to the hospital he was apparently unconscious, but could be aroused by pain; temperature 98.6°, and later in the day 104°; pulse, 76; respiration, 32; some weakness of left arm; skin dry and hot; pupils normal; hemorrhage from the left ear; large hæmatoma above the right ear; lacerated wound near the median line on the right side. Vesical control was lost for eight days. Incision of the hæmatoma disclosed a linear fracture extending downward and backward into the cranial base. From the second to the eleventh days he was much of the time delirious, often requiring mechanical restraint. When quiet he was at times rational in his speech, and at others irrational and had various delusions. From the twelfth day he had no more delirium, comprehension was slow, and delusions persisted. He thought his nurse was his school teacher, and that he had been at home at various times. These delusions continued at the time of his discharge from the hospital, on the twenty-second day.

In many cases of head injury the symptoms of mental disorder are sufficiently characteristic to make a recognition of left prefrontal lesion practically certain. In others, as previously noted, diagnosis remains conjectural unless death and opportunity permit postmortem inspection. The usual source of uncertainty in such cases is to be found in the more or less complete loss of consciousness, or in the delirium which attends general lesions. The loss of consciousness, if at all complete and persistent, proportionately annuls the mental activity upon which the diagnosis must depend; and active delirium is a result of general, not local, circulatory disturbances. Incomplete loss of consciousness or somnolence, however, must be distinguished from apathy, or from an entire abeyance of mental action, which are fairly indicative of destructive lesion of the subcortical tissue of the left prefrontal region. The early delirium of general contusion, or the later form which attends meningeal inflammation, must be discriminated from the mental aberrations which result from the localized (focal) lesion. It is impossible to formulate definite rules for differentiating delirium from abnormal mental states dependent upon the specialized local injury. It may be said, however, that a distinctly active delirium on the one hand, or a low muttering delirium on the other, is always

a general symptom, though the latter may result from a septic frontal laceration. The diagnostic mental disorders are delusions, emotional disturbances, mental enfeeblement, loss of memory, or impairment of other individual intellectual faculties, changes in character, etc., appearing early or late.

There is a form of alcoholic mania which, occurring after an injury of the head and in connection with well-marked previous symptoms, may be almost identical with traumatic dementia. There is also a condition of hysterical mania which, under similar circumstances, may raise a question in diagnosis.

The two cases which follow are instances of these forms of mania simulating that resulting from the prefrontal lesion, and will serve as illustrations of such sources of possible error.

Numerous more characteristic instances of mental disorder with recovery may be found in the published series of cases before mentioned.[1]

CASE D.—A woman, aged twenty-three years, fell ten feet from a roof to the ground, struck upon her head, and was stunned. On admission to the hospital she was conscious: temperature, 97.8°; pulse, 58; respiration, 20; profuse hemorrhage from both nostrils and subconjunctival hemorrhage in both eyes; both pupils unequally dilated and immovable; lacerated wounds of face and neck; linear fracture running from left parietal eminence to left external angular process, where it was lost. One hour later she was delirious, with lack of vesical and rectal control; one hour later still her mental condition was normal and her temperature rose to 101°. On the second day her mental condition was still normal and vesical and rectal control was regained; temperature, 102°. During the next two weeks temperature was only moderately elevated, with no general symptoms except widely dilated pupils, which contracted very slowly on exposure to the strongest light. Ophthalmic examination showed hyperæmia of the margins of the optic disks. At the end of this time she developed facial erysipelas, lasting for several days. After the day of her admission her mental condition had remained entirely normal. Three days after the subsidence of the erysipelas she had a sudden access of delirium of an hysterical character, without appreciable cause and without physical symptoms. Her speech was silly and her facies fatuous. Her delirium soon became maniacal and her mood melancholic, and for three weeks following her mania was constant, and she was noisy, excited, and the prey of constantly shifting and continuous delusions, which were usually of a painful or horrifying character. She thought, for example, that her father was being crushed; that her father or sister were about to be shot; that someone had thrust a dagger into her body. The ringing of a bell to her was the sound of a pistol shot, and the noise of a carriage passing in the street caused her to

[1] Phelps, Injuries of the Brain. 1897-1900, pp. 537-81.

scream in terror, because her father was being run over and killed. She talked constantly with invisible persons. Her pulse, temperature, and respiration remained nearly normal. At the end of this period the character of her delusions changed. They were scarcely less varied than before, but they were all of a happy or joyous nature. She was still excited, but laughing or smiling and happy. She was in fancy the bride of one of the members of the staff, and to his annoyance this delusion was rather persistent. She began taking food freely, which she had previously refused. At the close of this fourth week of her mania it ceased as suddenly as it had begun. She became entirely rational and remembered many of her delusions.

CASE E.—A man aged fifty-four years was admitted to St. Vincent's Hospital who had fallen in the street while intoxicated. He had received a lacerated wound in the right occipital region through which no cranial fracure could be discovered. The pupils and sensation were normal and there were no disorders of the muscular system. His mental condition was sluggish, temperature 100°, pulse 80, and respiration 24. At the end of a week's time he was transferred to the Bellevue Prison Ward. During this week his pulse rate and temperature were but moderately increased—99°, 96°, 70°. His mental condition was notably bright and alert, but his conversation was mumbling and incoherent, with delusions, and his comprehension was defective. In the second week his mental condition deteriorated. His delusions increased in number, he carried in his pocket an old glove stuffed with rags, which he imagined was his pocketbook and money. He followed the house surgeon about the wards and made imaginary notes of cases. His mind was still active and no new physical symptoms developed. He was then transferred to the erysipelas ward, where he died from an intercurrent pneumonia two weeks later.

It was learned from the man's family after his death that he had been the proprietor of a drinking place, and that for three years past he had been a hard drinker, and on two or three occasions had suffered an attack of delirium tremens or of some other form of alcoholic mania.

Necropsy. Comminuted and slightly depressed fracture involving upper part of left greater wing of sphenoid and adjacent borders of frontal and parietal bones; linear fracture extending from one-half inch to right of torcular Herophili to middle of groove for right sigmoid sinus; no intracranial hemorrhage; no subarachnoid effusion; laceration of right occipital lobe at site of occipital fracture.

"Microscopic examination of the segment of tissue removed from the left prefrontal area shows a universal hyperplasia of the connective tissue surrounding and supporting the smaller bloodvessels; in some places this has apparently resulted in partial obliteration of the perivascular lymph space. The walls of the vessels proper show also a certain amount of connective-tissue increase, par-

ticularly in the subendothelial layer. The glia tissue about these vessels shows a slight amount of thickening, but in other places appears to have been more or less macerated, as though from local œdema. There is no general sclerosis demonstrable and practically no changes of the glia tissue in any respect, except as stated about the vessels.

"Most of the ganglia cells appear normal, but a few show more or less atrophy and chromotolysis, occasionally with the deposit of brown pigment about the nucleus. These findings are in no way characteristic, but are such as might be found in any brain the bloodvessels of which show a chronic arteriosclerosis; alterations like these are commonly seen in the brains of chronic alcoholics. (Brooks.)

The origin of the mental disturbances in the second case was not fully determined until after the death of the patient. His antecedents were unknown, and a question of alcoholism was raised only because there was something in his mental condition somewhat different from what is usually observed in cases of traumatic dementia. The absence of gross lesions in the prefrontal region and the microscopic findings seem to warrant the final conclusion that the dementia was alcoholic. The hysterical nature of the mental disorder in the first of these cases was easily recognized. The fact that the condition was maniacal rather than one of dementia, and the practically complete subsidence of general symptoms of traumatism before the occurrence of mental disturbance, as well as the existence of characteristic features of hysteria, scarcely left room for doubt. In a case where some physical signs of injury still persisted, and in which the peculiarities of hysteria were less evident, diagnosis might well become more difficult.

The inferences to be derived from these histories are so similar to those which have been drawn from the cases of the earlier series, and the arguments in support of the contention of an exclusive left frontal localization have been so fully stated in a still recent publication,[1] that no extended comment is necessary. The cases are too few in number to warrant independent conclusions, but they are scarcely less important as affording cumulative proof of propositions already advanced. The addition of the present series of eleven cases to the forty-six previously published, making fifty-seven in all, seems to afford an adequate basis for positive opinion. While a limited number of cases of only negative significance have been included in order that the record of the writer's personal observations may be complete, there is not one which can be regarded as contradictory of the assertion that centres controlling intellectual manifestations are situated only in the left prefrontal area. A careful collation, as exhaustive as possible, of all cases of frontal lesions, published in the leading British and American journals,

[1] Localization of the Mental Faculties in the Left Prefrontal Lobe, THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, April-May, 1902.

and in some others, during the past fifteen to twenty-five years, has corroborated the conclusions deduced from an analysis of those observed by this writer. Mental aberration or decadence has attended nearly every implication of the left prefrontal lobe when normal consciousness has been retained, and has been absent in nearly every instance of limitation of the lesions to the opposite side. A very small number of cases of left prefrontal lesion have been reported, of which it has been asserted that the mind was unaffected, and of right prefrontal lesion, in which it has been said to have been disordered. The greater number of these have been found to be unworthy of credence; either no detailed history having been afforded, or the assertion found to be incompatible with the history as stated. An analysis of such cases of mental impairment with right frontal lesion, and of alleged mental integrity with left frontal lesion, collated prior to 1902, was made in the monograph[1] of that date. Since then seven additional instances of apparent anomalous mental conditions with frontal lesion have been reported. A similar analysis of these later cases afford the following results:

1. Glioma involving inferior one-half or two-thirds of right frontal lobe; patient irrational, noisy, and violent; was an epileptic. No note of condition of left frontal lobe was made.[2]

2. Traumatism of mesial and inferior surfaces of right frontal lobe in the prefrontal region; two years later, after great heat exposure, patient became epileptic with progressive mental enfeeblement and changes of character.[3]

3. Tumors growing from dura mater displacing and occupying position of first and second right frontal convolution; primary epilepsy and mental decadence.[4]

4. Tumor of right frontal lobe, with mental disorder; no note made of left frontal condition.[5]

5. Tumor of right frontal lobe; apathy and somnolence.[6]

6. Syphilitic tumor of right frontal lobe destroying its greater portion; mental disorder, especially affecting the "affective relations;" epilepsy; no reference made to condition of the left frontal lobe.[7]

7. Tumor of right frontal lobe, the removal of which left an enormous cavity; same phase of mental disorder as in preceding case; epilepsy; no reference to condition of left frontal lobe.[8]

The patients in five of these seven cases were epileptics; another had no mental disorder except somnolence and apathy; and a fifth was syphilitic. All these mental derangements were indicative

[1] Phelps. Left Prefrontal Localization, ibid., April-May.
[2] Revue neurol., 1902, Lejeune.
[3] Erskine and Shover. British Journal of Mental Science, 1901, p. 544.
[4] Honiger. Dominion Medical Monthly, 1902, vol. xviii. p. 92.
[5] Hunt. Journal of Nervous and Mental Disease, 1902, p. 227.
[6] Dercum. Ibid., 1905, p. 106.
[7] Durante. British Medical Journal, 1902, p. 1822.
[8] Ibid.

of general, not local, cerebral changes. In four the condition of the left frontal lobe was not examined, or at least not mentioned. No one of them can be regarded therefore as an exception to the general rule thus far established as to the negative results of right frontal lesions.

During the same period, from 1902 to 1905, inclusive, there were reported in the same journals twenty-three instances of exclusive right frontal lesion, mainly tumors and traumatisms, in which no mental disorders existed. During the same period again, in sixteen instances of exclusive left frontal lesion, the total number reported, some form of mental disorder was noted in every one. It is possible that some one or more isolated cases of lesion of either lobe may have escaped attention, but such a possibility is insufficient to invalidate the result.

The examination of surgical literature covering so long a period is not an easy task, but has been necessitated by the peculiar difficulties which attend this special cerebral localization.

The inability to infer largely from experimentation upon the lower animals, and the complexity of intellectual manifestations, both in their normal and morbid states in man, preclude the brilliancy of method not less than of result which has characterized the determination of centres of control for motion and other less-complicated functions, and render an exhaustive examination of available records of cases, together with careful clinical and pathological observation our sole reliance.

In view of the amount of evidence now accumulated, and in the absence of invalidating facts, it should be no longer possible to avoid the positive conclusion that control of the mental faculties resides in the left to the exclusion of the right prefrontal lobe.

It has seemed unnecessary to question the fact that the psychical centres are localized in the anterior rather than in the middle or posterior regions of the brain. This view is maintained by the majority of more recent writers upon the subject—*e. g.*, Bianchi, Burr, and Mills—and is fully corroborated by the necropsies upon which the present study of a special localization is based, though still denied by Clapham,[1] Campbell,[2] and some others. It has been demonstrated further not only in the cases which have been here quoted and detailed, but in numerous other cases of a different character, that lesions limited to the posterior left frontal region, comprising the ascending frontal and bases of the other frontal convolutions, occasion only motor defect.[3]

It has remained therefore only to determine in what part of the prefrontal region, if in any, the psychical centres are specialized.

[1] British Journal of Mental Science, 1904, p. 651.

[2] Ibid., 1902, pp. 9-11.

[3] British Medical Journal, vol. ix. p. 536; Brain, vol. i. p. 250; ibid, vol. xiv. p. 296; and all cases of simple motor aphasia.

The results of this inquiry may be summed up in syllogistic form somewhat more positively than in the monograph of 1902.

1. Mental decadence always attends conjoint lesion of both prefrontal regions.

2. Mental decadence always attends lesion of the left prefrontal region alone.

3. Mental decadence never attends lesion of the right prefrontal region alone.

These premises and the inevitable conclusion result from adequate clinical and parallel necropsic observation, which, as already stated, can alone suffice to determine this particular point in cerebral localization. Such cases as Andral's, Bailey's, Bramwell's, Gall's, Porta's, and Thibaudiere's, of almost entire destruction of the right frontal lobe or hemisphere, on the one hand, and, on the other, many of those detailed or quoted in the monograph previously cited, are absolutely demonstrative and not to be controverted except by the production of some equally well authenticated antithetical case.

The possible existence of exceptional cases in which mental default might be found to follow lesion limited to the right frontal lobe, or mental integrity retained where lesion involved the left prefrontal lobe, was considered in the former study of this subject, already quoted.[1] As then stated, such exceptional instances, if found to exist, would not be inconsistent with the fact that centres of control for mental processes are exclusively located in the left prefrontal lobe, since many cases have been recorded in which functional anomalies have been found to be dependent upon anomalies of cerebral structure. Many well-known instances were cited to which may be added more recent cases of Eddinger[2] and Collins,[3] in the first of which removal of the entire left temporal lobe was followed only by temporary right hemiplegia and "doubtful hemianopsia," and in the second of which the lesion (abscess) and manifestation of motor symptoms were on the same side.

The nature of these centres—the manner of their action in controlling mental processes—is immaterial to the present purpose. It is here simply a question of topography, the determination of an anatomical substratum for mentation, as it has already been determined for speech and motion.

It will be noted in all the cases of left prefrontal lesion cited, save seven, that death resulted at an early period, being delayed in only two instances a little beyond the first month, and in a majority occurring within ten days. In the exceptional cases the prefrontal region was atrophied in four, was the seat of abscess in two, and in one, which, as a matter of convenience, was included in the series of traumatisms, was the seat of a tumor. One of the

[1] Phelps. Prefrontal Localization, etc., p. 45.
[2] New York Medical Journal (editorial), 1902, vol. lxxvi. p. 333.
[3] Journal of Nervous and Mental Disease, 1903, vol. xxx. p. 569.

seven terminated in death at the end of thirty days, and the others only after the lapse of years.

In the cases of recent occurrence and early fatal termination laceration is the characteristic frontal lesion; but it is not conceivable that the destruction of tissue is the cause of death, nor is it certain that it determines the characteristic mental disorder. It is probable that the laceration is rather an indication of the amount of general disturbance of cerebral nutrition or of a more limited local disturbance; the one causing death, and the other an abnormal condition of the psychical centres. It this be true a simple left prefrontal contusion with its resulting hyperæmia and œdema, if of sufficient gravity, should be attended by similar mental disturbances. In two instances of local excessive hyperæmia and œdema, to which reference was made in an earlier publication,[1] this actually occurred. These were the only such instances out of 225 cases observed and verified by necropsy, in all of which circulatory disturbances existed. If the general circulatory derangement is only moderate in degree the cerebral symptoms are but slight and give no evidence of implication of the cortical centres; if excessive, all specific functional disorders are lost in unconsciousness or delirium, conditions which have been regarded as indicative of lesion of the cerebral cortex, as a whole, and referred with the pulse and temperature to the class of general symptoms. It is not inconceivable, however, that at least one of these—delirium—may be a local manifestation of the general lesion, or rather of that part of it which implicates the left prefrontal centres. The exceptional instances quoted may give this speculation some support; but the fact that all parts of the brain are at the same time involved in the common vascular derangement would seem to make impossible that attribution of a particular symptom to any limited area.

If the prefrontal laceration is limited to the cortex its effect is to derange the mental processes, but not to limit their activity. The cells suffer in their nutrition, but are not necessarily subject to macroscopic change. If the patient soon recovers it may be supposed that the error in nutrition has been remedied, or that if cell degeneration has already begun it has ceased and normal cell formation has been re-established. It may happen that early symptoms of cortical laceration are at a little later period gradually or suddenly replaced by stupor and coma. In such cases small vessels either in the cortex or subcortex which have been ruptured and from which the primary hemorrhage has been insignificant, have continued to bleed until the cerebral tissue has been suddenly or gradually disintegrated with a corresponding change in symptoms. If the lesion is confined to the subcortex stupor or coma will be primary symptoms. So in the case of lesion confined to the right prefrontal

[1] Phelps. Injuries of the Brain, p. 136.

area, a primary normal mental condition may in like manner be followed by similar failure of consciousness.

The smaller number of cases in which life is somewhat prolonged with progressive mental decadence, or the larger number of those of congenital idiocy, in both of which classes cerebral atrophy is a characteristic feature, are susceptible of more positive histological explanation. In both instances atrophy usually involves the whole cerebrum. In the traumatic cases it is most marked in the frontal region and usually in the left prefrontal portion, indicating not only the general contusion and hyperæmia in which it originated, but its greatest intensity in the part in which the psychic centres are situated. Both cells and neuroglia indicate constructive as well as destructive changes. The pathogenical process beginning in an active hyperæmia seems to terminate in a true cirrhotic inflammation. There is a marked neurogliar and cellular hyperplasia, and a production of new and imperfectly formed capillaries in both gray and white matter. At the same time the pyramidal and polymorphic cells of the several cortical layers show various types and stages of cytoplasmic and nuclear degeneration, with spaces of tissue rarefaction. A detailed account of these appearances in a typical case is given by Dr. Brooks in his examination of the brain in Case X. of the monograph of 1902. Bolton believes that in cerebral atrophy changes occur chiefly in pyramidal cells, and pre-eminently in the prefrontal region, "which subserves therefore the psychical or associated centres."

The destructive tissue changes in case of abscess formation or tumor, due to inflammation and compression, require no present consideration. In fact any histological study is foreign to the simple topographical problem which has confronted us.[1]

It is only in exceptional cases, if any, that external compression, even to the extent of flattening the lobe, impairs the integrity of the mental processes. In a single instance in which the frontal lobe was compressed by a large subarachnoid serous effusion there were mental disturbances which seemed to be so occasioned; but it is not certain that the compression was the sole cause of the nutritive changes, since such a localized effusion would imply an extreme degree of corresponding cortical hyperæmia either from contusion or inflammation.

The necessity of care in discriminating the mental derangements due to a general cerebral hyperæmia from the indications of a destructive prefrontal lesion was pointed out in the more detailed consideration of the subject in the previously quoted article of 1902,[2] and again in the immediately preceding pages.

NOTE.—I quote from a recent translation into English of Bianchi's *Text-Book of Psychiatry* (James H. McDonald, 1906): "An

[1] Histological Basis of Amentia and Dementia, London, 1903.

[2] Phelps. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, April-May, 1902.

exception to this rule would be found in the case of Phelps, who expresses an opinion that is not original, but still is of great interest. According to this author traumatic lesions of the frontal lobes, frequently of the left, are causes of grave specific and immediate mental disturbances." And, again: "The distinction between subcortical and cortical syndromes is not solidly based upon observation."

I desire to correct these errors, probably originating in the first translation from English into Italian, by the first of which I am inadvertently so entirely misrepresented by the distinguished author.

(1) My whole contention has been that such mental disturbances are due *exclusively*, not "frequently," to lesions of the left (pre) frontal lobe.

(2) The distinction I have made to which he alludes was expressly stated to be general, not absolute, as he seems to infer. It is perhaps immaterial whether the view I have maintained as to the exclusive function of the left prefrontal lobe is original, but I have been unable to discover a similar expression of opinion or suggestion by any previous writer.

ON "DOUBLE EGO:"

WITH REPORT OF AN UNUSUAL CASE.[1]

By Alfred Gordon, M.D.,

of Philadelphia,

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In ordinary conditions the ego is distinctly conscious of all the psychic processes that are constantly taking place. Self-consciousness is a *sine qua non* of normal life. When the self-consciousness becomes disturbed, the ego can no more witness properly the mental activities and the individual loses the power of criticism, of perceptions, of ideas and is consequently led to errors. In psychoses, in which the disturbances of consciousness play a most important role, the delusions are the direct result of the affected self-consciousness.

Disturbances of consciousness may manifest themselves in various degrees. The most typical form of all is *amnesia*. The person thus affected loses all remembrance of his previous life; he possesses a new ego. In some cases the patient passes through two or more different short periods of life as two or more personalities, and one is not aware of the existence of the other. However, in a certain

[1] Read and patient presented before the Philadelphia Neurological Society, October 24, 1905.

group of cases fragments of one personality are retained by the other; some acts committed during one state may be recalled in another state. There are, consequently, cases in which there is no real complete interruption but rather a continuity of consciousness which is only altered in its power of criticism at various periods. In another group of cases there is a profound disturbance of general sensibility, and the entire person thus affected speaks of himself in the third person.

The majority of cases of dual personality recorded in literature are examples of complete loss of normal self-consciousness, upon which normal sensory stimuli have no effect. The characteristic feature of them lies in the fact that the psychomotor sphere is not inhibited in either state. Each personality in its own state acts in response to inner stimulations, and one state has not the remotest association with the other. It may happen that the lives the two personalities lead are diametrically opposite to each other. As remarkable examples of such a state may be mentioned: the old celebrated case of Mary Reynolds (a case of double consciousness by Weir-Mitchell), and the more recent case of Rev. Mr. Hanna (multiple personality by Sidis and Goodhart). In the latter consciousness was so profoundly dissociated that the two personalities he presented before treatment was instituted, had individual systems of psychic states which carried on their functions in an absolutely independent manner.

All the cases of double or multiple consciousness recorded in the literature present almost the same feature, viz.: that at no special time there was a simultaneous coexistence of the two egos: one follows the other or they alternate. In Wilson's[1] case there were as many as twelve personalities, the transition of one to another was gradual or rapid, but only one at a time was in function. There is another common feature in the literature of these cases. At first there is total amnesia: one personality is unconscious of another; later, with or without treatment the gap separating the dissociated mental states is gradually getting narrower or filling up; some recollection of the past state appears in the mind of the patient in the successive state, so that after a long interval one state becomes aware of the existence of the other and the two egos may finally become synthetized into one personality. This is the usual process in cases of recovery. Those patients who do not recover present during their entire life the above-mentioned alterations of personalities with complete amnesia of each preceding state. The case I am about to report presents this common feature with other cases in that it began with attacks of *complete* amnesia. Gradually attempts were made to remind him of some acts done by him during the amnesic state and he recalled them in a vague manner. Later on he began to realize the existence of secondary states. The

[1] Journal of Mental Science, October, 1903, p. 640.

great interest of the present case lies in its unusual and remarkable termination, which makes it so different from all other cases that I feel warranted in reporting it before this Society.

The history is as follows:

Eight or nine years ago the patient, K. J. W., who was then nineteen years old, was accused by his mother of staying away from home two nights. Employed to sell tickets in a theatre, he was during those two nights at the ticket office as usual. He had no recollection of being absent from his home and was surprised when told so. He was also astonished when his employer reproached him afterward that certain new orders given at that time were not carried out by him. Since then the same disobedience was noticed several times and the employer wondered why he should accept the order in good faith, never refuse and then ignore it, while he had always been exact and correct in his work. He was therefore able to do the routine work without making the slightest mistake, but when told to do an act outside of his ordinary daily work he would not do it. Attacks of this "absent-mindedness," as he calls it, would occur quite frequently at the beginning. The duration of the longest attacks would be two days and four to five hours of the shortest. When repeatedly told that he was asked to do certain acts—as, for example, write letters or see a certain person, etc.—he would be greatly surprised and would beg for details, as he was anxious to know the reason of his "absent-mindedness." Once, for example, he sent his wife a telegram, but when reminded of it could not believe that he had done it.

At first he disbelieved the occurrences, but finally accepted them. Gradually he began to recall some facts which happened during these attacks, when persistently reminded of them, but they would appear to him as having occurred very long ago and at a great distance from him; however, at no time would he remember that he participated in any act or witnessed occurrences during the attacks. Being constantly reminded of this condition, he gradually recalled more and more facts, so that he finally began to realize that he passed sometimes through a "second state," as he expressed himself. He became so accustomed to it that he even expected them at any time.

About eighteen months after the onset, once while in the army during the Spanish-American war, he felt that an internal conversation was going on in him: "You are a fool, you can't do this or that." Since then the sensation occurred to him several times and every time that internal "being," as he called it, would always be opposed to his actions, or try to interfere a great deal and even suggest to him wrong doings. At first he would *feel* the other being rarely, but later quite frequently. He certainly tried to resist this internal opposition with great force and persistence, but the more he tried, the less he succeeded. This constant struggle brought

him gradually face to face with the second personality from which he is suffering now. At first the latter would appear only in spells, but gradually it became continuous and he was forced to accept its existence, to use his own expression. He believes that *his ego is double:* there is number one and number two. Moreover, number two is always antagonistic to number one. Whatever number one wishes to do, to say, number two will always take the opposite view and will interfere with the actions of number one, so that there is always a struggle for supremacy between the two egos. Ordinarily number one succeeds in overcoming number two, but sometimes the fight is so hard that number one succumbs and number two takes full possession of number one. On one occasion, for example, the patient suffered from toothache; a dentist applied to the tooth some medicine. When he arrived home, number two said to him: "I have got you now;" a fight ensued. Number one lost the battle and then the patient lost consciousness. His wife gives a good account of another attack. Suddenly he became excited, walked around in the room, saying: "It is going to get me," and then said loud: "Go away, there is a black tongue back of you which is going to take me;" his face was flushed, the eyes were watering, the mouth was frothing, he was trembling and apparently struggling; he was totally unconscious to the surroundings. He was put to bed. He slept a profound sleep. At 4 A.M. he was awakened, as he had to go to work at that hour, but he could not tell where he worked, could not recognize his relatives.

Number two is with him all the time; at his work; at home; on the street; it has now only a partial possession of him, but when full possession will take place, the patient believes, "it will be a case of insanity." The fight between the two egos is continuous, and the patient dreads hard fights in which number two attempts to take complete possession of number one. Nine weeks ago the two egos compromised. Number one promised to teach number two his business. In return number one will have the right to smoke and continue his work without being interfered with. As soon as number two learned the business, he broke the promise; refused to give number one his liberty and the conditions remained the same—namely, full possession is taken of number one by number two occasionally. Only recently he stayed away from his home nine consecutive nights, fully realizing the gravity of the deed, but was unable to overcome number two who had full possession of him. Only once he returned to his wife, and instead of expressing his regret he called her various names, shouted and yelled, then suddenly left. Questioned about his strange actions, he said that he fully realized the injustice to his wife, but it was number two that did it and number one had no power to restrain number two.

Besides the attacks which are the result of the struggle between number one and number two, the patient had spells of another

nature: on one occasion (last December), while going down in the cellar, he lost consciousness, and fell; his face was pale and he breathed heavily. Another spell: in the engine room several times he would look up for a moment without knowing what he was doing. He would also have spells, in which without provocation he would begin to talk rapidly, call his wife names, shake his fist in her face. Occasionally, while in bed, he would suddenly cease talking and lie motionless for a short while. In his shop he would at times forget what work to do next.

In the present state his condition can be summarized as follows: he is absolutely convinced that he is composed of two beings—number one and number two. The latter is inimical to the first in every respect; suggests wrong acts, interferes with his life, even dictates to him bad language when he talks to others; briefly, number two is always for "the bad part of life." It is constantly in him, cannot be separated from him, controls his actions and never leaves him for a moment. Patient has full knowledge of right and wrong and resists, therefore, the evil influence of number two. Most of the time he overcomes it, but sometimes number two overpowers number one and takes full possession of the latter. When number one loses the battle the patient enters into a state of unconsciousness. In his judgment number two is not a material being; he does not see or hear it, but he only feels its presence.

The existence in him of two egos and the fact that number two forms an integral part of his psychic life, led him to further deductions. He believes now that an identical condition exists in all human beings: "we are all composed of two egos; this is an inevitable condition of normal life." There is a difference, however, between his two egos and those of other individuals. Normally the two egos work in harmony; one does not attempt to overcome the other, and there is no such a thing as taking possession one of another. In his case the condition is morbid, he says, as number two is not equal in strength to number one; number two works for evil, number one for good. For this reason he consults medical men; the object of the latter is not to remove number one or number two, as they must exist, but only to endeavor to bring the two egos to an understanding, to make them work harmoniously, as in normal individuals. Furthermore, he believes that besides number one and number two there is a third element which controls the actions of both, and this is the function of the brain. The latter oversees the work of number one and number two.

Such is the mental attitude of the patient. He is intelligent, industrious, attends to his work correctly, never makes mistakes. He is an engineer, does responsible work, and never fails in doing his duties. His previous history is negative. Physical examination shows a marked tremor of the hands, absent knee-jerks, which can be brought out slightly by reinforcement, slightly unequal pupils.

No hysterical stigmata could be found. In the family history we can mention only that his father was alcoholic.

A close analysis of all the facts in this case shows that a *disturbed consciousness* is the fundamental pathological feature. The periods of amnesia, then the gradual transition into two separate states, the gradual recognition of their existence by the patient, the formation of two inseparable egos, one depending on the other, and the absolute belief in their presence to the extent of a delusion, finally attacks of loss of consciousness of very short duration on the order of certain forms of *petit mal*—all these symptoms are evidences of a disintegration or at least of disturbance of consciousness. It is the latter that forms the diseased element in the patient. That attacks of amnesia are psychic equivalents of epilepsy in a certain group of cases is now almost universally admitted. This fact, together with the genuine attacks of *petit mal* which the patient presents, makes it highly probable that epilepsy is the actual disease from which the patient is suffering. The patient's firm and irrevocable belief in the existence of two egos in himself and in all human beings, belief which has become a delusion—together with the above-mentioned facts—appear to me that we have to deal here with a form of *epileptic psychosis.*

This, so to speak, "epileptic view" could be applied to the phenomena of the dual state of our patient. The first intimation of the existence of number two he got when he heard suddenly an internal voice saying, "You are a fool, etc." Spells of this character occurred to him quite frequently, but always in spells. Finally their frequency made him accustomed to this condition and he became convinced of the existence of number two. Then he would have spells of fights or internal struggles with number two, but these spells were always preceded by provocations from number two in the form of an internal voice. A moment of reflection will tell us at once that we have to deal here with hallucinations which originate in one or several sensory centres. This is the so-called psychosensory hallucinations. The mode of their appearance (in spells), their sudden onset in the present case, remind us of motor epilepsy in relation to the excitation of the motor centres. We can therefore say that the hallucinations constitute here, so to speak, "an epilepsy of the sensory centres." What particular centre is in a state of excitation in this case is difficult to say (perhaps the auditory). Cerebral physiology teaches us that hallucinatory images are complex phenomena, as various sensory centres are in a certain relation to each other.

With these few remarks I merely wish to show that in my opinion the epileptic nature of all the phenomena of the case presents a great degree of probability.

I may also mention that, since the condition had been recognized as such, an appropriate antiepileptic treatment ameliorated the

condition; for several months there was no more occasion for number two to take possession of number one and there was no recurrence of attacks of amnesia or of other forms of *petit mal* until a few weeks ago.

In conclusion I wish to emphasize again that this case is unusual and probably unique as an example of *coexistence* of two egos at the same time.

I wish to acknowledge my indebtedness to Dr. E. L. Klopp for the privilege of studying his case.

THREE CASES OF TRAUMATIC BROWN-SEQUARD PARALYSIS.

By Julius Grinker, M.D.,

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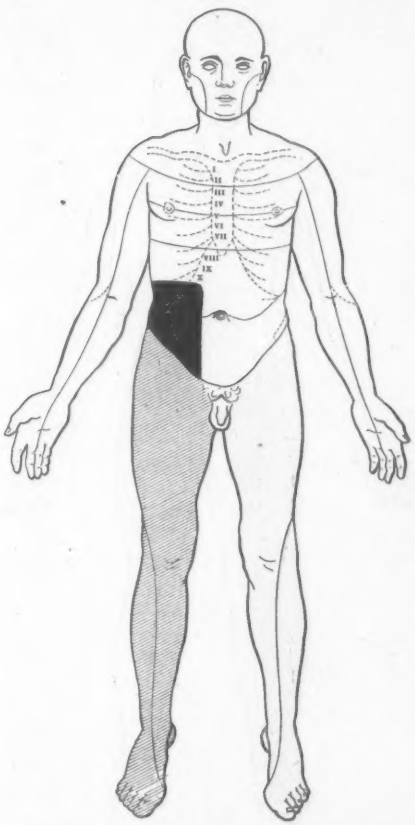
Within the past three months it has been my privilege to study three cases of injury to the cord, each presenting a somewhat different etiology, but all having in common the well-known Brown-Séquard syndrome. Case I. presents the classical type and, like the first cases described, was caused by a stab wound. Case II. demonstrates an incomplete syndrome, produced as a result of fracture dislocation of the dorsal spine; while Case III. illustrates a fairly complete Brown-Séquard syndrome as part of the symptoms of a cervical hæmatomyelia.

Before relating the histories of my cases, it is necessary to summarize what is understood by the Brown-Séquard syndrome. The great French physiologist, after whom the symptom-complex was named, as early as 1849 described the symptoms of a lesion of one-half of the cord substantially as follows: Motor paralysis and hyperæsthesia of the same side as the lesion, and anæsthesia of the opposite side. With the motor paralysis on the side of the lesion may be associated normal or exaggeration of the various forms of sensation, an anæsthetic zone in the upper portion of the lesion, and frequently a zone of hyperæsthesia above this, hyperthermia and paralysis of the sympathetic, arthropathies, and muscular atrophy. On the side opposite the lesion we find paralysis of sensation affecting mostly the pain and temperature senses; to a lesser degree tactile sensation. The sensory disturbances do not begin quite as high as on the side of the lesion; voluntary movements are normal on this side, and the muscle sense is usually preserved. An enumeration of the causes that may produce the Brown-Séquard syndrome will include trauma, such as fracture,

dislocation, hemorrhage, bullet wounds; or disease, such as vertebral arthritis, limited to one-half of the cord, spinal thrombosis, meningitis, hemorrhage, syringomyelia, tumor, or syphilis.

CASE I.—J. S., an Austrian laborer, aged twenty-four years, entered Cook County Hospital September 14, 1905.

FIG. 1

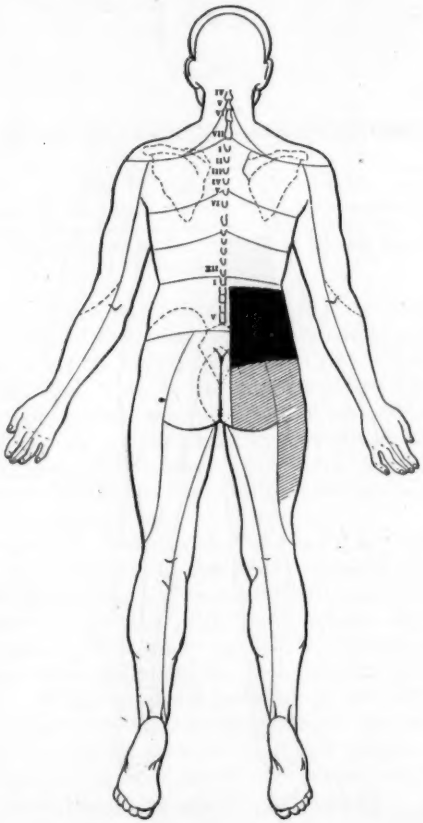


Tactile sensation. Black area—complete anæsthesia. Shaded portion—hypæsthesia.

History. About five months ago, during a quarrel in which knives were used, he sustained a stab wound in the middle of his back, and several large and some small flesh wounds upon the posterior portion of the right thigh. Almost immediately thereafter a complete paralysis of motion appeared in the right lower extremity, which compelled him to remain in bed three months. Improvement

was slow, but he gradually began to use his limb, so that now he is able to walk without a cane. Almost from the beginning he complained of pains in his right thigh and leg, which still persist, although in a mild form. The entire left lower extremity feels cold since the accident, and sensation in this limb is either perverted or entirely abolished. At no time have the sphincters been involved.

FIG. 2

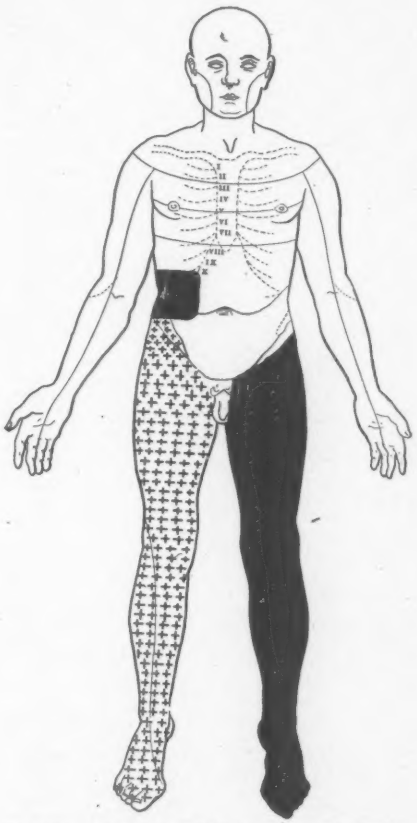


Tactile sensation. Black area—complete anæsthesia. Shaded portion—hypæsthesia.

Examination. The patient is well nourished, of average weight and height, and presents several scars, evidently the remains of injuries sustained five months ago. One of these, larger than the rest, about three by five inches, is seen on the outer portion of the

right buttock; the others are scattered over the upper portion of the right thigh. A medium-sized scar is found on the right side near the median line, between the sixth and seventh dorsal spines. He points to this spot as the exact location where the knife penetrated the spinal cord.

FIG. 3



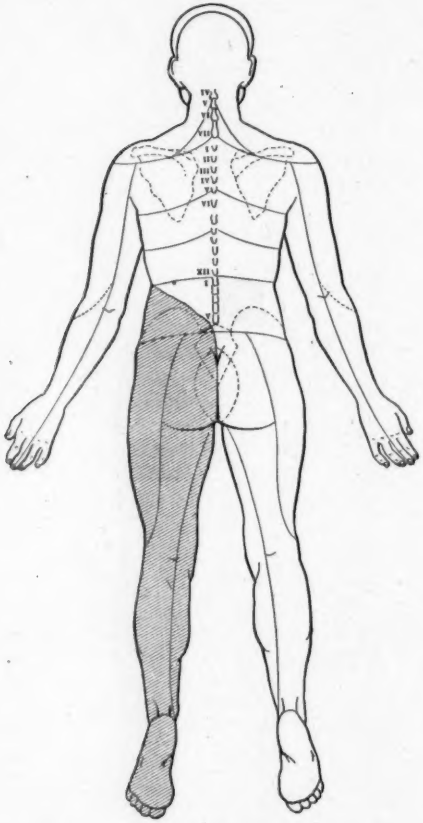
Pain sense. Black area—analgesia. Stars—hyperalgesia.

The viscera were found normal in every respect; glandular enlargements could not be detected; no anomalies of sensation or motion were discoverable in the face and neck. The palpebral fissures were equal on both sides; also the pupils, which reacted promptly to light and in accommodation. There is no wasting or paralysis of any of the muscles of upper extremities, trunk, or abdomen.

The left lower extremity appears to be of normal volume and strength.

The right thigh and leg show considerable atrophy, but this seems to affect the limb uniformly. Strength is considerably reduced and spasticity is marked.

FIG. 4



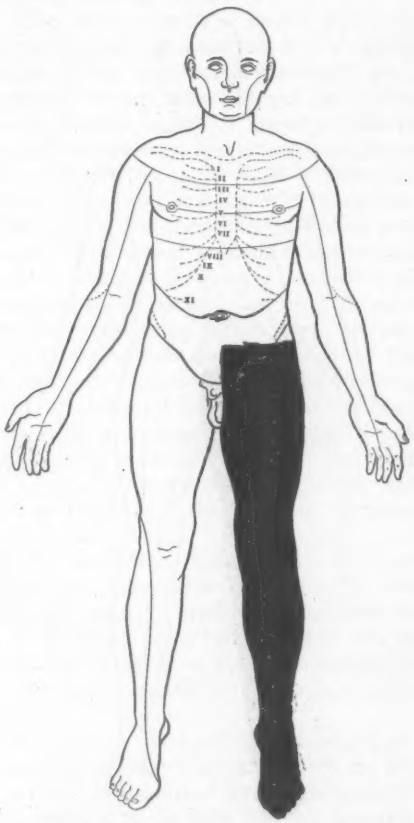
Shaded portion—hypalgesia. Unshaded lower extremity should have been marked X, showing hyperalgesia.

Reflexes. (*a*) *Superficial.* The abdominal reflex cannot be obtained on either side. The cremaster reflex is active on the left and slightly reduced on the right side.

(*b*) *Deep.* On the left side the knee-jerk and Achilles phenomenon cannot be elicited, even with reinforcement. On the right side

the knee-jerk and Achilles jerk are exaggerated, ankle clonus is present, and typical Babinski, Oppenheim, and Gordon signs are in evidence. In testing the lower extremities for inco-ordination the left is found normal, but the right limb is distinctly ataxic and presents various degrees of muscle and joint-sense disturbance.

FIG. 5



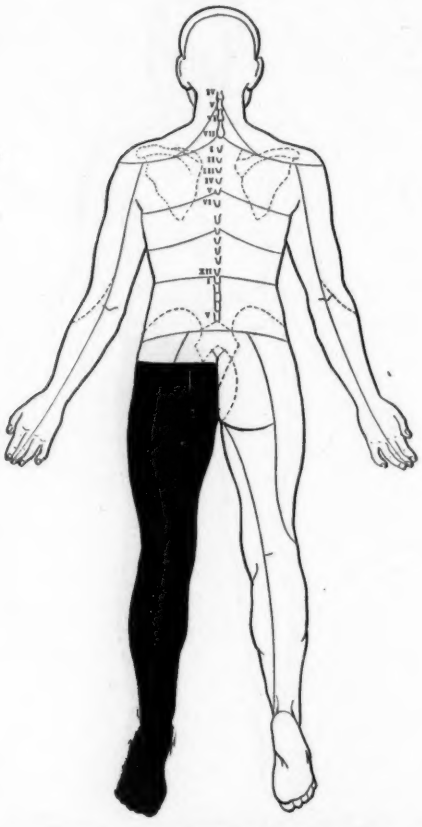
Temperature sense. Black area—thermoanæsthesia.

Sensation. (*a*) *Tactile.* The right lower extremity shows marked hypæsthesia, beginning at the groin and involving its entire anterior surface and the upper portion of the thigh posteriorly. From the end of the right costal arch to the beginning of the right Poupart ligament there is complete anæsthesia, which involves a correspond-

ing area posteriorly. The left lower extremity and left half of the trunk are perfectly normal to touch. (See Figs. 1 and 2.)

(*b*) *Pain: Right Side.* A slight pin prick is instantly perceived as an intense pain; this hyperalgeasi is found in the entire lower extremity up to the inguinal fold, and extends all around the limb. A strip of anæsthesia, two and one-half by three inches in width,

FIG. 6



Temperature sense. Black area—thermoanæsthesia.

extends half around the trunk and is superimposed upon this hyperalgesic area.

Left Side. There is complete analgesia on the anterior surface of the left lower extremity up to the inguinal fold. The external and posterior surfaces are only hypalgesic. (See Figs. 3 and 4.)

(*c*) *Temperature.* The right side is sensitive to cold and heat. The entire left lower extremity shows almost complete thermo-anæsthesia, beginning at the highest point of Poupart's ligament and extending almost circulatory around the left half of the body. (See Figs. 5 and 6.)

An examination made October 24, 1905, reveals practically no change in findings, except that the left knee-jerk, previously unobtainable, is present, although reduced,

SUMMARY. The case presents a motor paralysis of the right lower extremity and a sensory paralysis of the opposite limb.

The right-sided motor paralysis is essentially an upper neurone palsy, with spasticity, exaggerated reflexes, ankle clonus, Babinski, Oppenheim, and Gordon signs; of sensory disturbances on this side, we find loss of muscle sense and impairment of tactile sensation.

The left side presents sensory paralysis of pain and temperature, with preservation of tactile and muscle sensation. A strip of analgesia on the right half of the trunk, including the area supplied by the ninth and tenth dorsal segments, approximately indicates the situation of the lesion in the cord. According to our tables of localization, the ninth and part of the tenth dorsal segments are found between the seventh and eighth dorsal vertebræ, which are opposite the sixth and seventh dorsal spines, and this is the exact location where the stab wound was received by the patient. The case just reported is really a duplicate of some of the classical cases described by the early writers on Brown-Séquard paralysis.

The remaining two cases occurred in the Neurologic Clinic of the Northwestern University Medical School, and I am under obligation to Prof. Hugh T. Patrick for his permission to publish them.

CASE II.—L. C., an Italian fruit peddler, single, aged forty-one years, came under my observation November 20, 1905. His family history is good; both parents, brothers, and sisters are well. With the exception of "growing pains" at the age of ten years and rheumatism, followed by smallpox in 1893, the patient always enjoyed good health. He never drank to excess and never contracted venereal disease.

In 1882 he fell from a chestnut tree, a height of about twenty feet, and became unconscious for about ten or fifteen minutes. When picked up he complained of intense pains in the lower spine, and it was discovered that his right leg had become paretic. For thirty days following the accident catheterization had to be resorted to in order to relieve urinary retention, but the rectal sphincter had never been affected. In the course of four months the patient was sufficiently well to resume his occupation, but his right leg continued to feel stiff and clumsy, and dragged considerably in walking. Practically no change has occurred in this respect during all the years since the accident. A sensation of constant lameness in his

spine, he states, has gradually yielded to the application of liniments. He never had a girdle sensation, but about a year ago he began to experience occasional cramp-like pains in the calf muscles of his left leg, which were either caused or aggravated by walking. Of late he suffered from rheumatic pains in his left elbow-joint, and from occasional headaches and dizziness; also from neuralgic pains encircling his left knee.

Status Præsens. Patient, a well-developed man of average height and weight, with no abnormalities about face and upper extremities, is seen to drag the right leg in walking, his gait resembling that of cerebral hemiplegia. The right lower extremity is slightly smaller than the left, but there are no localized atrophies. The paretic limb is spastic to the point of lead-pipe rigidity, and the deep reflexes are exaggerated. Ankle clonus, Babinski, Oppenheim, and Gordon signs are present.

The left lower extremity shows no noticeable impairment of motility, but there is slight spasticity, with Babinski, Oppenheim, and Gordon signs. There is no atrophy, and the knee-jerk is greatly reduced.

Sensation. (*a*) The test for *tactile* sensation reveals a small strip of hyperæsthesia, beginning a little above the right knee and extending on the outer side of the leg for about two-thirds its length anteriorly and about two-thirds the width of the leg posteriorly. The skin over the right big toe is also hyperæsthetic.

On the left side there is slight impairment of tactile sensation on the entire anterior surface of the leg and a small area just above the knee. Posteriorly, touch is about normal.

(*b*) *Pain and Temperature Sense.* Beginning midway between the umbilicus and the inguinal line, which corresponds to the upper level of the eleventh dorsal segment, there is thermoanæsthesia and analgesia involving the left half of the body from above downward, and including the entire left lower extremity. The thermic has suffered more than the algesic sense.

The right lower extremity shows a small area of thermohypæsthesia and hypalgesia, which is about one inch wide and extends from a little above the knee to the termination of the upper third of the leg.

Upon inspection of the spinal column we discover a distinct projection beginning at the ninth dorsal and including the third lumbar vertebra. The spinous processes of these vertebræ seem united by a new bony formation, which has completely immobilized this portion of the spinal column. The patient indicates the upper border of this ankylosed area as the seat of his former pains.

An examination of the vascular system, blood, and urine revealed normal conditions.

SUMMARY. A previously healthy individual sustained injuries to his spine by a fall from a tree, which resulted in motor paralysis

of the right lower extremity, with slight sensory disorders on this side, but with distinct loss of temperature and pain sense and some impairment of tactile sensation on the opposite side. A kyphosis and ankylosis of vertebræ mark the site of injuries, which were evidently in the nature of a fracture dislocation, which has damaged the right half of the cord more than the left, and in this wise produced an incomplete Brown-Séquard paralysis.

How can we explain the exaggerated reflexes and the other signs of pyramidal tract involvement which were discovered on the left side? Either by assuming the development of an exostosis within the spinal canal, similar to the one visible outside, which probably irritates the left crossed pyramidal tract and the posterior roots, and thus causes the exaggerated reflexes and the neuralgic pains encircling the left knee, or by supposing that both halves of the cord were unequally affected by the original injury; the right more than the left. Whichever view one may hold regarding the chronological development of symptoms, we have an incomplete Brown-Séquard paralysis due to fracture dislocation, with the upper level of damage at the eleventh dorsal segment.

Case III.—A. B., aged twenty-three years, male, telegraph operator, with good family and personal history, was first seen by me on November 29, 1905. He states that on October 26, 1905, while asleep in a baggage coach of a moving train, he was suddenly awakened by a collision, then became semiconscious and dazed. While in this condition he was taken from the wrecked train, and for several days thereafter he could only with difficulty be aroused to take food. He gradually emerged from this state, and, when sufficiently rational to give an intelligent account of his symptoms, he complained of great pain in the cervical region of the spine, particularly over the vertebra prominens, and of pain and paræsthesia in hands and fingers. During the next few days he was powerless to use any part of his body, but within a week the left side began to improve, and ten days later he could also move the right side of his neck; still later some power returned in the right leg and arm. These last seem to have borne the brunt of the injury, as they are still weak and paretic. Over the left frontal bone, beginning anteriorly at the junction of the skin and hair, and extending in an anteroposterior direction for about two inches, a scalp wound was discovered, which healed and left a big scar. The skull evidently was uninjured.

Status Præsens. A pale young man of slender physique is seen to drag his right foot in walking. With the exception of an ugly scar over the left frontal region, the head and face reveal no abnormalities. The shoulder girdle appears considerably flattened out, particularly the right side. The patient can barely raise his arm over his head, but is unable to hold it there for even a few seconds. The right pectoral and serratus muscles, with a portion of the right

trapezius, have become atrophic, and impairment of functions in them is easily demonstrated by the usual tests. The right triceps muscle is flabby and wasted; to a lesser extent the left triceps; both biceps muscles are in fairly good condition. The right forearm is thinner than normal posteriorly, and the right thenar eminence is considerably reduced in size. The right first interosseous space is abnormally deep, but the left also appears to have suffered somewhat.

The right lower extremity is slightly thinner than the left, and is paretic. The deep reflexes on this side are exaggerated, and Babinski, Oppenheim, and Gordon signs, as well as ankle clonus, can be readily obtained.

The left upper and lower extremities show no marked impairment of motor function and no apparent wasting, with the exception of slight atrophy in the serratus and some deficiency in the biceps muscle. The knee-jerk is decidedly reduced on this side.

The paretic and atrophied muscles do not show the typical formula of the reaction of degeneration, with the exception of a slight qualitative change evidenced by a somewhat tardy response to both currents.

Sensation. Tactile sensation seems normal everywhere. Beginning at the third rib on the left side and extending circularly around the left half of the body, and including the entire left lower extremity, there is a distinct loss of pain and thermic sense, although temperature is more nearly abolished than pain sense. There is apparently no involvement of the ciliospinal centre.

SUMMARY. The peculiar combination of symptoms presented lead one to infer damage to the cervical gray and injury to the right pyramidal tract destined to reach the right lumbar cord. As regards motor functions, we have noted paralysis and atrophy of muscles at the shoulder girdle and of the right arm and forearm, and to an insignificant extent, also, of the left upper extremity. Besides there are unequivocal signs of implication of the right crossed pyramidal tract as manifested by paresis, with spasticity and exaggerated reflexes, without atrophy in the right lower extremity. And finally we have a typical sensory dissociation—viz., the preservation of tactile, and either reduction or extinction of pain and temperature sense in the entire left half of the body below the third rib. This constitutes a Brown-Séquard syndrome, in that there is motor paralysis on the right and sensory paralysis on the opposite side. But we also have atrophies in the upper extremities. Applying our anatomical knowledge and the history of the case to correlate the symptoms, we can satisfactorily explain all the phenomena by assuming the existence of a hemorrhage into the cervical cord, which has invaded the right side more than the left, and in this manner only incidentally produced the Brown-Séquard syndrome.

As this is merely a clinical report, I do not intend to discuss the theoretical considerations regarding the exact etiology of this interesting symptom-complex. It is sufficient to state that the exact causation is still unexplained, but we hope that even this will be satisfactorily elucidated when we have gained more certain knowledge of the normal course of the sensory fibres within the spinal cord and brain. It is reasonably certain, however, that for the production of the Brown-Séquard syndrome it is essential that one-half or a portion of one-half of the cord be affected, and also that the sensory fibres, either in the central gray or after they have crossed over to the opposite Gowers tract, be implicated in the pathological process. As has been seen by the preceding report, which emphasizes the traumatic element, and as can be learned by consulting other reports which lay stress upon disease as a causative factor, it matters little whether that process is traumatic or produced by disease. It may not be amiss to add that the finding of this syndrome always establishes the existence of organic changes in the spinal cord, as opposed to functional and cerebral diseases.

HEMOPHILIA IN THE NEWLY BORN, WITH REPORT OF A CASE.

By Ralph C. Larrabee, M.D.,
of Boston.

The etiology of uncontrollable hemorrhages in the newly born is a subject which has caused much discussion. Early writers attributed it to various degenerative diseases and congenital defects. It was associated with jaundice in 84 of the 220 cases reported by Grandidier in 1871. In many of his cases inherited syphilis existed; and the work of more recent writers has shown the same fact (Mracek, Hess), though the exact relationship between the two conditions is not clear. It has also been attributed to injuries to the vasomotor centre in the brain (Pomorski).

In most cases, however, there is reason to believe that the condition results from bacterial infection. Many organisms have been demonstrated at autopsy or by blood cultures during life. They include both of the staphylococci, streptococcus, pneumococcus, bacillus pyocyaneus, B. lactis aërogenes, B. coli communis, and perhaps others. Organisms possibly specific have been isolated by Klebs, Gaertner, Kilham and Mercelis, Weigert, Dungern, Hamill and Nicholson, and Mapes. In the cases of several of these writers the isolated organisms inoculated into animals have produced hemorrhages. It does not seem probable that all cases

are due to the same organism, and, indeed, the part played by bacteria in the process is not well understood.

The view that the disease is directly dependent upon specific bacterial infection is strongly supported by its relative frequency in lying-in hospitals. Townsend, for example, found that out of a large number of babies born in the wards of the Boston Lying-in Hospital 0.57 per cent. suffered from hemorrhagic disease; while among the babies of patients of the same institution born in their homes it occurred in but 0.10 per cent. Definite hospital epidemics have occurred, such as the one reported by Kilham and Mercelis in the New York Infirmary for Women and Children. Again, most cases run a course like that of an acute infectious disease—those that do not die from the immediate effects of the hemorrhages recover completely, and show no further tendency to unusual bleeding. These considerations are compatible with an explanation of the condition on the basis of bacterial infection.

So much attention has recently been given to the infectious cases that the occasional occurrence of the disease as a manifestation of true inherited hemophilia has been to a degree lost sight of. Some, indeed, have denied that hemophilia ever occurs in the first days of life. It is true that the first manifestations generally appear in later infancy or early childhood. But this rule is subject to frequent exceptions, as the most cursory inspection of the literature will show. Grandidier, in 1872, had collected 228 cases of spontaneous hemorrhages from the navel in the newborn, and of these 14, or 6 per cent., occurred in hemophilic families.

The accompanying table includes the 14 cases of Grandidier, and such further ones as could be found in the more recent literature. A case has been accepted as hemophilia (*a*) if there was a distinct history of this disease in the family, or (*b*) if the baby recovered from the first hemorrhage, but in after life remained a bleeder. Much difficulty was experienced in deciding whether to include certain cases. In several instances, without other evidence of inherited taint, two or three successive children of the same mother have died of hemorrhages in the early days of life. These were not included. Many cases do not appear to have been personally observed by the authors who reported them, but were probably accepted on the authority of some patient or his friends in giving his family history. In some it is merely stated that the patient, first seen in later childhood or adult life, "bled from birth." On these grounds doubts may be expressed as to the cases of Holton, Dunn, Gayet, Sahli, and the second of Faludi. These have been included for the sake of completeness. Their omission would not materially affect the conclusions.

Together with the case presently to be described I have found thirty-seven instances of true hemophilia in the newborn, representing twenty-four families.

CASES OF HÆMOPHILIA IN THE NEWLY BORN.

No.	Reporter.	Sex.	Family history	Sources of early hemorrhages.	Remarks.
1	Elsässer. Hufel Journ., Bd. lviii.	M.	Hemophilic.	Umbilical cord.	Died.
2	Bicking. Ibid., 1837.	...	"	Cord or navel.	"
3	Quadrat. Oester. med. Woch., 1841.	...	"	Navel, gums, skin.	"
4	Burdach. Med. Vereinszeitung, 1836, No. 4.	...	"	Navel, finger, groin.	" } same family.
5	" " " " " "	...	"	Umbilical cord.	"
6	Elsässer. Hufel Journ., 1833, Bd. cxxii.	M.	"	Umbilical cord, scrotum.	"
7	Wachsmuth. Die Bluterkrankheit, 1849.	M.	"	Umbilical cord.	"
8	" " " "	M.	"	" "	" } same family.
9	" " " "	M.	"	" "	"
10	Vezin. Casp. Vierteljahrsbr. ger. Med., 1855.	M.	"	" "	"
11	Vogel. Lehrb. d. Kinderkrankr., 1838, Heft 7 & 8.	M.	"	Navel.	"
12	Spahn. Schmidt's Jahrb., Bd. cxxxix. p. 172.	M.	"	Umbilical cord.	Recovered, but died of hemorrhage at age of 7.
13	Reinert. Virchow u. Hirsch Jahrsb., 1869, ii. 269.	M.	"	" "	Died.
14	Storrs. Prov. Med. and Surg. Journ., 1842.	F.	Probably hemophilic.	" "	Recovered, but remained a bleeder } sisters.
15	" " " " " " "	F.	Probably hemophilic.	Navel.	" " " }
16	Hochstetter. Virchow's Arch., 1863, xxviii. 426.	M.	"	"	" " "
17	Brigstock. Brit. Med. Journ., 1872, vol. ii. p. 122.	M.	Hemophilic.	Skin and joints.	" " "
18	Holton. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1874, vol. lxvii. p. 414.	M.	"	Umbilical cord.	Died.
19	Dunn. Ibid., 1883, vol. lxxxv. p. 68.	F.	"	Nose.	Recovered, but remained a bleeder } same
20	" " " " " "	F.	"	"	" " " } family.
21	" " " " " "	M.	"	Not stated.	" " " }
22	" " " " " "	M.	"	Umbilicus.	Died.
23	" " " " " "	M.	"	Nose, kidneys, bowels, joints.	Recovered, but remained a bleeder.
24	Gayet, Gaz. hebdom., 1895, xxxii. 258.	M.	Not hemophilic	Not stated.	" " "
25	Comby. Gaz. des hôp., 1896, lxix. 793.	F.	Hemophilic.	Nose, skin.	" " "
26	Brook. Trans. Lond. Clin. Soc., 1901, xxxiv.	M.	"	Umbilical cord.	" but continued a bleeder } same
27	" " " " " " "	M.	"	" "	" died hemorrhage age 1 year } family.
28	Faludi. Arch. f. Kinderheilk., 1904, xxxix. 92.	M.	"	Circumcision wound.	" " " 6½ yrs. } brothers.
29	" " " " " "	M.	"	Nose.	Died; prematurely born bro. of No. 28 }
30	Lossen. Deut. Zeitschr. Chir., 1905, lxxvi. 1.	M.	"	Skin.	" } same
31	" " " " " "	M.	"	Umbilical cord.	" } family.
32	" " " " " "	M.	"	" "	Recovered, but died hemorrh. aged 2¾
33	Sahli. Zeitschr. f. klin. Med., 1905, lvi. 264.	M.	"	Stomach.	Died }
34	" " " " " "	M.	"	Intestine.	" } same family.
35	" " " " " "	M.	"	"	" }
36	" " " " " "	M.	"	"	" }
37	Larrabee. Case herewith reported.	F.	"	Navel, nose, skin, bowels, vagina.	"

An analysis of the table shows that in 22 cases the baby died, but there was a clear family history of hemophilia. In 4 the family history was negative or unknown, but the child recovered and continued to be a bleeder. Gayet's patient is the only one in which the family is positively stated to be non-hemophilic. This case of undoubted hemophilia was not observed until later childhood, and the account of hemorrhages immediately after birth is so meagre that it must be placed in the doubtful class. The remaining 11 were positive by both criteria.

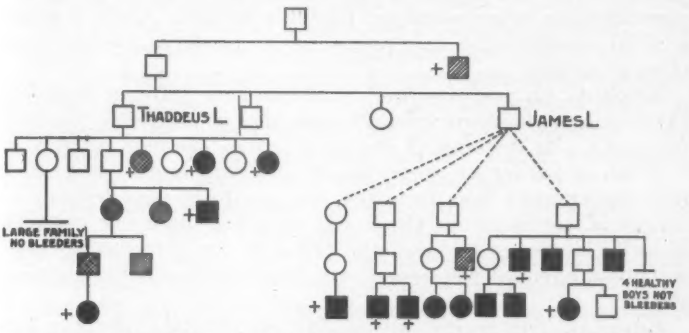
The mortality was 60 per cent., which should be compared with the mortality of 62 per cent. in Townsend's infectious cases. The occurrence as to sexes is according to the usual rule for hemophilia, all but 6 out of 33 being males, and in contrast to the commoner infectious cases, in which about as many females as males are affected. The most common site of hemorrhage was the umbilicus or umbilical cord (23 cases, in 19 of which it was the only site). Other sites were skin (7 cases), nose (6 cases), bowel (4 cases), joints and genito-urinary tract (2 cases each), operation wound, gums, and stomach (1 case each). In 2 the site was not stated. Although several writers state that circumcision is often the occasion for the first hemorrhage, I have been able to find but 1 case where this occurred under circumstances admitting of no doubt as to etiology.

The following case is reported because of its bearing on the etiology of hemorrhagic disease of the newborn, and because the occurrence of the case by sex and the hereditary transmission is not according to the usual rule for hemophilia:

Dorothy L. was born March 18, 1904. The mother had had a miscarriage about two years before, twins born at six and one-half months. There was no suspicion of syphilis. The case was referred to me by Dr. Charles W. Gardner, of Boston, who attended the confinement and had charge of the baby afterward. The child was born at full term. Labor was normal, the vertex presenting in the left occipito-anterior position. When dilatation was complete the membranes were ruptured artificially. During the process a minute scratch was made on the baby's scalp, and the hemorrhage from this was never controlled. The child weighed five pounds and appeared perfectly normal. The cord was tied in the usual way, but after a few hours a small hemorrhage appeared at the cut end. It continued irregularly, in spite of several ligatures. On the second day nose bleed took place, then hemorrhage from the rectum, the stools being large and black, with some bright-red blood. On the same day purple spots began to appear on the face, and later elsewhere. Blood came from under the finger-nails, and even appeared to ooze from the unbroken skin. Prostration was marked and the temperature constantly subnormal. On the fifth

day there was a copious hemorrhage from the vagina, and soon after the baby died.

The body was seen by the writer a few hours after death. No autopsy was made. The skin presented innumerable dark hemorrhagic spots, varying in size from a pea to a silver dollar. No other abnormality was detected.



The squares indicate males, the circles females, solid black signifies bleeders, diagonal shading slight or doubtful cases, crosses indicate that the patient died of hemorrhage.

For the following family history I am indebted to the grandmother of the patient:

David L. (first generation) came to America from England about 1757. The cause of his death is unknown, but there is a tradition that his brother, Kirvin, bled to death. David L. had four children—Thaddeus, Lucy, Ephraim, and James (second generation). None of them were themselves bleeders, but numerous bleeders existed among the descendants of Thaddeus and James.

Thaddeus L. (second generation) had three sons and six daughters (constituting the third American generation), of which the following died of hemorrhage: (1) Female child, lived twenty-four hours, and died of hemorrhage from the nose and rectum. (2) Louisa L. was throughout her life subject to violent nose bleeds. At the age of forty-two years she had a sudden, severe hemorrhage from the uterus and died after an illness of three days. (3) Angeline L. died at the age of thirty-five years of hemorrhage after the removal of a tumor. Neither of these women had children.

David H. L. (third generation), one of the sons of Thaddeus, died of hemorrhage into the brain at the age of sixty-two years. He had two daughters and a son (fourth generation): (1) Henry L. died at the age of twenty-one days of hemorrhage from the navel, nose, skin, and ears. (2) Louisa L. suffered from severe and repeated hemorrhages from the nose in the early weeks of life. In after years she manifested no especial tendency to hemorrhage. She died of cancer at the age of forty-five years and left no children.

During her last few years she had serious trouble with the knee-joints, which finally became so swollen and stiff that even after death they could no be straightened. (3) Nellie A. L. also had serious hemorrhages from the nose in the first three weeks of life. After the birth of her first child she flowed for six weeks. After her second confinement she had such a severe hemorrhage that she almost died. She is still living and well at the age of fifty-two years and has never considered herself a bleeder. Quite recently a trivial wound of the scalp with a hatpin produced a hemorrhage of some severity.

Nellie A. L., just described, had two sons (fifth generation). (1) Edwin L. had two severe hemorrhages in childhood resulting from cuts. As the scars of these are in the vicinity of arteries, it is by no means certain, even though physicians in attendance had difficulty in controlling them, that they are to be regarded as evidences of hemophilia. He is still alive and does not consider himself a bleeder. (2) A son, who died at the age of nineteen of consumption, attended with severe nose bleed and pulmonary hemorrhage.

Edwin L. (fifth generation) has had one daughter, Dorothy, the child who is the principal subject of this paper, dying of multiple, spontaneous hemorrhages at the age of five days.

Returning now to James L. (second generation), we find that among his numerous descendants the hemophilic tendency is even more marked than in those of his brother Thaddeus, already described. I am unable to trace their lineage with the same accuracy but the following fragments are well vouched for.

A certain Charles P. lost a son at the age of three weeks from nose bleed. Every effort was made by the doctor to stop it, but, though temporarily successful, it kept recurring until death ensued. His sister suffered for three years before her death from a disease of the knees resembling tuberculosis. She died at the age of twenty-five. The maternal grandmother of this child was a descendant of James L., probably a daughter.

Another grandson or greatgrandson of James L., bearing his family name, lost two sons of hemorrhage. One bled to death at the age of eighteen years, after the removal of a tooth. The other cut his hand at the age of seven and, in spite of medical attention, he died from the resulting hemorrhage.

Still another L., a descendant of James, is said to have bled to death. His sister has two daughters, still living, who are recognized bleeders. They bleed profusely if they receive the slightest scratch, and great care is being taken to guard them from accidents.

A. L., another descendant of James, had a large family which presents exquisite examples of hemophilia. His widow, still alive, states that all her male children show the tendency to a greater

or less degree. When cut, even slightly, severe bleeding follows, often stopping only when the child faints. Sometimes a cut heals promptly, and then a painful, dark-colored mass appears. If this is opened severe hemorrhage again occurs. A. L. had eight sons and a daughter. One son died in early childhood of hemorrhage from a trivial cut on the lip made by a chip of wood. Two of the seven boys still living are recognized to be marked bleeders. Another, Lewis L., himself not considered a bleeder, has two children. The daughter resembled the L.'s in feature and died a few hours after birth. She had a profuse eruption of purple spots and a large black swelling on the scalp. The son resembled the mother's family in features and has never manifested the hemophilic tendency. The only daughter of A. L. has never shown any unusual tendency to bleeding, but she has two sons who are bleeders.

In this family, besides the case observed, we have a history of four infants dying of hemorrhage within a few weeks of birth. Moreover two women, one of whom is still living, suffered from severe epistaxis in the first weeks of life. One of them continued a bleeder for many years, though in the slight degree characteristic of female hemophilics. The other had chronic joint disease of a severe type. The objection that these histories are merely family traditions is perfectly valid, and for that reason they are not included in the table. Yet, though the records of competent medical observers are not at hand, too much confirmatory evidence has been obtained to admit of a doubt as to the main facts.

It must be concluded that while most cases of hemorrhagic disease of the newborn are of bacterial origin, there is at least one class of cases sharply to be distinguished from them—namely, those due to hemophilia.

Apart from the interest attaching to this case as one of hemorrhagic disease of the newborn in a hemophilic family, it is significant in that the transmission is not according to the usual rule. This familiar rule is to the effect that males alone suffer from the disease, but that they do not transmit it to their offspring. Women, on the other hand, do not manifest the disease themselves, but, if they are members of hemophilic families, may transmit it to their male children. In the family herewith reported there have occurred fifteen known cases of hemophilia, of which six were females. Moreover, of these 15 cases 10 inherited the disease through a male parent. These figures do not include the 7 which were of slight severity, or concerning which the history is so meagre that they must be considered doubtful.

It is probable that the true proportion of cases bearing the L name, and hence inheriting the disease from the father, is smaller than these figures would indicate, since it has been impossible to get detailed information concerning the families of female members Genealogies are interested in the male line almost wholly. In othe

words, this history includes the exceptional and irregularly inherited cases, while those transmitted in the usual way are to a large extent lost sight of.

Several cases appear from the chart to have inherited the disease through a non-hemophilic father, an occurrence admittedly rare. But it must be remembered that most of these cases are recorded as not being bleeders merely because their histories are unknown. Besides, bleeders often conceal their trouble. It is not probable that inheritance from a non-hemophilic father occurred so often in this family as the figures seem to indicate.

In the light of modern theories of inheritance it is difficult to account for the transmission of any character in the way common to hemophilia. In spite, however, of the *a priori* improbability of such occurrences, too many cases have been observed to admit of a doubt. Still the rule has many exceptions. According to Grandidier, about one bleeder in thirteen is a female. Several recent writers consider the preponderance of males much less marked. Faludi states that nearly a third are females. It would appear that in some families the occurrence as to sexes and the inheritance is strictly according to rule, as in the cases of Sahli and Lossen. In others the occurrence as to sexes is irregular, as in the cases of Fischer, Goodall, Blaker, Pearson, Steiner, Dunn, Türk, and Reinert. Steiner's cases were particularly bizarre, as only females suffered and the disease was transmitted directly from mother to daughter, males neither inheriting the disease nor transmitting it. In some families the rule of transmission only through the female is frequently broken, as in the case mentioned by Litten, in which the fathers transmitted the disease directly to the sons through three generations. The irregular transmission in our case, therefore, and the frequency with which females were affected, are by no means unprecedented.

In conclusion it should be repeated and emphasized that this paper deals with the exceptional cases and that hemophilia is but a rare cause of uncontrollable hemorrhages in the newly born. The importance of this is obvious. Given an infant suffering from this condition, the chances are all in favor of its being due to a cause which is but temporary. No effort should be spared to save the child, since if it survives for a few days there is every probability of continued health.

References.

Blaker. British Medical Journal, 1904, vol. i. p. 189.
Dungern. Centralblatt f. Bakteriologie, 1893, Bd. xii.
Dunn. The American Journal of the Medical Sciences, 1883, vol. lxxxv. p. 68.
Faludi. Archiv f. Kinderheilkunde, 1904, Bd. xxxix. p. 92.
Fischer. Centralblatt f. Medicin, 1890, Bd. xi. p. 186.
Gaertner. Archiv f. Gynäkologie, Bd. xlv. p. 272.
Goodall. Scottish Medical and Surgical Journal, 1905, vol. xvi. p. 133.
Grandidier. Die freiwilligen Nabelblutungen der Neugeborenen, 1871.

Grandidier. Schmidt's Jahrbücher der Medicin, 1863, Bd. cxvii. p. 329; 1872, Bd. cliv. p. 81; 1877, Bd clxxiii. p. 185.
Hamill. Archives of Pediatrics, 1903, vol. xx. p. 265.
Hamill and Nicholson. Ibid., 1903, vol. xx. p. 641.
Hess. Ibid., 1904, vol. xxi. p. 598.
Kilham and Mercelis. Ibid., 1899, vol. xvi. p. 161.
Kiebs. Archiv f. experimentelle Pathologie und Pharmakologie, 1875, vol. iv. p. 473.
Litten. Nothnagel's Encyclopedia of Practical Medicine.
Litten. Deutsche Klinik, 1903, Bd. iii. p. 421.
Lossen. Deutsche Zeitschrift f. Chirurgie, 1905, Bd. lxxvi. p. 1.
Mapes. Quoted by Holt, Diseases of Infancy and Childhood.
Mracek. Archiv f. Dermatologie und Syphilis, 1887, Bd. xix. p. 117.
Pearson. Lancet, 1904, vol. i. p. 91.
Pomorski. Archiv f. Kinderheilkunde, 1892, Bd. xiv. p. 165.
Reinert. Jahresbericht, 1869, Bd. ii. p. 269.
Sahli. Zeitschrift f. klinische Medizin, 1905, Bd. lvi. p. 264.
Steiner. Johns Hopkins Hospital Bulletin, 1900, vol. xi. p. 44.
Townsend. Archives of Pediatrics, 1894, vol. xi. p. 559.
Türk. Centralblatt f. innere Medicin, 1902, Bd. xxiii. p. 208.

PULMONARY GANGRENE FOLLOWING FOREIGN BODIES IN THE BRONCHI.

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The condition of pulmonary gangrene was first recognized and accurately described by Laennec,[1] whose classification of the diffuse and circumscribed varieties holds to this day.

Traube,[2] in 1853, in a full article, further divided the disease according to its origin: (1) in the bloodvessels, (2) in the bronchi, and (3) in pre-existing disease of the lung parenchyma. The vascular origin may be due either to an infected embolus or to a simple infarct, becoming infected subsequently from the air passages.

The second class, that of gangrene originating from the bronchi, includes those cases secondary to putrid bronchitis or bronchiectasis, and the aspiration gangrenes. These latter are due to the inhalation of foreign matter, either liquid, semisolid, or solid. Liquid materials may come from any part of the upper air or digestive tracts. Besides infected foods, many other things have been mentioned, such as putrid material from the mouth during operations on carcinoma of the tongue or larynx, or necrosis of the jaw, from the secretion of typhoid perichondritis of the larynx, or from perforation of diverticula or cancer of the œsophagus. The

semisolid substances are usually food materials, while the variety of the solid bodies is limited only within the range of substances which an individual may put into the mouth.

The third class of Traube—namely, gangrene occurring in the site of a pre-existing pathological process of the lung parenchyma—includes those cases following pulmonary abscess, chronic pneumonia, tuberculosis, and traumatism.

The subject which we wish to consider here is that mentioned in Traube's second class, and only a narrow subdivision of that—namely, the gangrene caused by the occurrence in the bronchi of solid foreign bodies.

The various writers on the subject of pulmonary gangrene speak of foreign bodies in the bronchus as a cause, in such terms as not rare, common, or frequent. This fact does not seem to be borne out by a study of the literature. Gross,[3] in his classical monograph on *Foreign Bodies in the Bronchus*, Poulet,[4] in his extensive study in Wood's *Library*, and Weist,[5] in a collection of 1000 cases of foreign bodies in the air passages, do not mention gangrene as a sequel; and Hoffmann,[6] in Nothnagel's *System*, in his table of 252 cases, mentions it only twice; while Murphy[7] in his article on "Surgery of the Lung," in a collection of 59 cases of gangrene, does not give foreign bodies as an etiological factor; and careful search of the literature reveals but 31 cases, which appear in the accompanying table. In one article,[8] in which a large table of the results of foreign bodies in the air passages is given, gangrene is mentioned as a quite frequent sequel. A perusal of the originals of the articles there collated, however, showed in several cases evidence of gangrene too meagre to enable the authors to include them in the present series.

An analysis of these 31 cases shows that the foreign body was a tooth twice, a pin once, a piece of wood once, a button twice, a head of grain or grass seven times, a bit of evergreen twice, a fruit-stone twice, a bone ten times; not mentioned four times; that it occurred with equal frequency in adults and children; that it remained in the bronchus before gangrene set in from four days to five months, usually under three weeks. The analysis further shows that the gangrenous process lasted from three days to four years, most frequently from two to four weeks; that the right lung was involved in 14 cases, the left lung in 7 cases, and that the outcome was death in 21 cases, recovery after thoracotomy in 2, and spontaneous recovery in 4 cases, and that the foreign body was coughed up in 5 cases, 4 of which subsequently died, and 1 made a rapid recovery. At postmortem examination the foreign body was found in 15 cases; in 11 of these it was still in the bronchus, and in 4 it had perforated into the cavity in the lung parenchyma. The most striking point brought by this analysis is the proportion of cases in which the exciting material was organic to those in which it was a mineral

substance. This, when it is considered how frequently coins and other metallic articles are swallowed and inhaled by children, would seem to point to something intrinsic in the foreign substance itself as a factor in the determination of the development of gangrene, and that the mere pressure and irritation effects of the body are not the only factors.

As to the diagnosis of this condition we are able to add nothing new. In several cases there was no history of the inhalation of the foreign body, but the signs and symptoms of gangrene were present. The presence of the characteristic putrid odor to the breath and sputum are certainly the most constant symptoms of pulmonary gangrene, and the only ones on which a diagnosis can be made. This even may not be constant, as is shown by case eleven, in which Robertet[18] states that there was a foul odor neither to the sputum nor to the lung at postmortem examination, a fact attributed by him to the complete obstruction of the bronchus, and consequent failure of secondary infection from the air. The cough, dyspnœa, pain, and fever are in no way characteristic of gangrene. It appears, then, that there is nothing absolutely diagnostic of this condition, and that a mistake in diagnosis may be unavoidable. It would seem, however, that in all cases of pulmonary gangrene the probability of the occurrence of a foreign body in the bronchus should be considered, and that when the evident signs of gangrene are accompanied by a total absence of breath and voice sounds over the affected area, even in the absence of a confirmatory history, the presence of a foreign body should be strongly suspected.

The mortality of this condition is great, due not only to the gangrene, but also to the difficulty of removing the exciting cause. When a definite diagnosis has been made there may be some hope of benefit from thoracotomy, but the results have been, on the whole, unsatisfactory, and fatal terminations have occurred, even when the exciting cause has been removed.

The following case, which has recently been under the authors' observation, is reported in full as an addition to the meagre literature on this subject.

The patient, J. B., male, aged thirty-seven years, was admitted to the Lakeside Hospital on July 12, 1905 (Medical No. 4832). Service of Dr. Edward F. Cushing.

He was sent to the hospital with the provisional diagnosis of typhoid fever. Being a Roumanian and unable to speak English, French, or German, no history was obtainable during life, except that he had been sick for ten days, and was suffering from headache, feverishness, and pain in the right side.

On subsequent investigation among the patient's friends the following data were obtained:

He was quite well until July 1st, eleven days before admission. During the meal that evening he accidentally "swallowed" a piece

of bone, and was immediately seized with a violent paroxysm of coughing, with occasional slight expectoration of blood. He complained of severe pain, felt deep in the right chest and radiating to the back. This was continuous, but increased with the cough. The cough was practically constant for four days, preventing sleep, and abated only on exhaustion. At this time he complained of a feverishness, and feeling sick all over, and rapidly lost strength. From then on the feverishness increased, the pain became more general, and the cough less frequent, supposedly due to increasing weakness. No expectoration was noticed. The appetite was lost; chilliness and sweating were prominent features after the first week. The patient grew rapidly worse until sent to the hospital. Until the present illness he had always been a hearty, robust man, and a very moderate user of alcohol.

On examination the following conditions were noted: A large-framed, rather thin man, lying quietly in bed in a somewhat apathetic condition, breathing easily, but somewhat rapidly, 36 per minute; no cough; pulse regular, rhythmic, 84 to the minute; good volume and low tension, not dicrotic; vessel walls not palpable. Systolic blood pressure 118 mm. of mercury by the Cooke modification of the Riva-Rocci instrument; temperature was 104°; the mucous membrane fair color; skin slightly moist; eyes normal; teeth showed quite marked pyorrhœa alveolaris; throat normal; tongue moist, red, and tremulous, lightly coated with a white fur. The breath is slightly musty, but not offensive. Axillary, epitrochlear, and inguinal glands palpable. The thorax is well built, symmetrical, costal angle is good width, the expansion is good, though slightly diminished on the right side. The left lung, except for a few large bronchial rales scattered throughout, is clear on palpation, percussion, and auscultation. The right lung is clear in front. In the lower axilla and back the percussion note is somewhat impaired, and the breath sounds, though diminished in intensity, have a normal vesicular character. In lower right lobe, over an area the size of a silver dollar, in the midaxillary line is a definite friction rub. The heart is normal in size and position; the heart sounds are clear. The abdomen is slightly distended. The liver dulness extends from the sixth rib in the right mammary line just to the costal border. The edge cannot be felt. The spleen can just be palpated. The genitalia and legs are normal.

The discrepancy between the temperature and the pulse, with the apathy and headache and palpable spleen, seemingly strengthened the suspicion of typhoid fever; the patient was treated accordingly. For two days the temperature varied from 102° in the morning to 104° toward evening; the pulse remained below 100, and the respiration came down to 24 per minute. The leukocyte count was 14,800, hæmoglobin 83 per cent., and the Widal reaction quite negative. The urine was dark amber and cloudy. Specific gravity 1020, acid

in reaction, and contained faint traces of albumin, a few leukocytes, and occasional hyaline and granular casts.

On the night of the third day in the hospital, July 14th, the patient began to cough considerably. The only change in the physical signs was a slight increase in the area of the friction rub. This evening the patient was seen to be perspiring profusely.

On the morning of the fourth day a decided change was discovered in the patient's condition. He looked more ill. The pulse had risen to 110 and the respirations to 30. He was drenching wet from perspiration, and in a violent paroxysm of coughing. With each paroxysm he raised large amounts of a greenish-brown sputum, of so offensive an odor that it was easily detected at the other end of the ward, and the patient had to be removed to a room by himself. The report of the examination of the sputum, made by Dr. John Phillips, follows: About 200 c.c. of sputum was coughed up in twenty-four hours, standing in a conical glass it separated distinctly into three layers—an upper frothy, a middle moderately clear, and a lower layer consisting of grayish sediment. The frothy layer was of a grayish-brown color. The odor was very offensive. On microscopic examination the sputum was found to consist chiefly of detritus, with many leukocytes scattered throughout. No bacteria beyond a few cocci were seen. On boiling with sodium hydrate, and examining the sediment, an occasional shred of elastic tissue was seen. The sputum was negative for tubercle bacilli.

On examination of the chest on this day the percussion was unchanged, except for a cracked-pot note in lower axilla; the breath sounds were somewhat blowing in character over the right back and over this same area there were very many large bubbling rales. The friction rub could no longer be heard. The vocal fremitus was below normal. An exploratory needle driven well into the lung below the angle of the scapula, and again in the posterior axillary line, failed to obtain anything more than 2 c.c. of bloody serum.

On the following morning, the fifth day, the patient appeared distinctly worse. His temperature remained unchanged; his pulse was 124, and respiration 40. He continued to spit up the same foul sputum. On examination the right chest was seen to be fuller than the left, the right measuring 43.5 cm., the left 41.5 cm. at the nipples, and the intercostal spaces to be bulging; the excursion of this side decreased. On percussion the entire right front and axilla were tympanitic from the clavicle to the costal border, the thoracic area of liver dulness being obliterated, and the lower border of the liver having moved from the costal border to the navel. The percussion note in the back remained unchanged. The vocal fremitus was markedly increased over right upper front, and slightly above normal in axilla and back. The breath and voice sounds were everywhere feeble. Succussion and coin sounds could not be obtained. The heart remained in its normal position.

Author.	Sex and age.	Foreign substance.	History.	Symptoms	Latency of gangrene.	Duration of gangrene.	Signs.	Site of foreign body.	Results.
1.* Langlet [4]† 1776, from Barbeu-Dubourg.	M.	Bone.	Sucking marrow bone; cough, pain, hæmoptysis.	Dyspnœa, cough, vomiting, fetid sputum.	.....	.....	.....	.....	Died; coughed up bone, relief from symptoms, but sank rapidly; left lung gangrenous.
2. Gilroy [10] 1831.	F. 40	Piece of chicken bone.	Inhaled during meal; violent cough, suffocation.	Depression, soreness, paroxysm of cough, hectic fever, profuse sputum.	36 days.	47 days.	.....	Right breast near bifurcation of trachea.	Died 83 days; gangrenous abscess of right lung, 20 oz. red-brown fluid.
3. Lawrence [11] 1838.	M.	Vertebra of fish.	Swallowed eight days before admission; nausea and vomiting.	.....	8 days.	24 days.	.....	Bifurcation of right bronchus.	Died 32 days; many gangrenous cavities in lung.
4. Brown [12] 1850.	F. 21	Bone.	Swallowed Dec. 20th; dry cough; pain Jan. 14th, fever, pneumonia, dyspnœa.	Jan. 16, sudden, profuse, stinking, mucopurulent expectoration; bone expectorated.	26 days.	15 days.	.....	.....	Died 39 days; gangrene of left and middle lobes right lung fetid cavities; right lung normal.
5. Brown [12] 1850.	M. yo'ng	Bone.	No symptoms for three weeks.	Pain right side; profuse, stinking expectoration; hectic fever.	3 weeks	Short.	.....	In abscess of right lung.	Died 21 days; gangrenous abscess in lower lobe right lung.
6. Struthers [13] 1853, from Barbeu-Dubourg.	M. 22	Bone 1 cm. long.	While eating soup; white sputum, cough five months.	Fetid and bloody sputum two years, then improved for two years, then fever, dyspnœa, cough, and fetid sputum.	5 mos.	4 years.	Dulness right side, vocal resonance, bronchi and sibilant râles.	Bifurcation of right bronchus.	Died in 4¼ years.
7. Hildreth [14] 1853.	M. 17	Twig of red cedar.	Immediate cough, pain right side, bloody sputum.	Ninth day pain, rigors, fever.	10 days.	6 days.	Dulness right front below fifth rib; breath sounds lost; bronchophony rales.	Abscess cavity of right lower lobe.	Died 16th day; rt. pneumothorax, gangrene rt. lower lobe.
8. Rothmund [15] 1853, after Gresner.	M. 16	Ear of grass.	Chills on next day.	Expectorated putrid gland with elastic tissue.	9 days.	8+ mos.	.....	.....	Recovered in one year.
9. Hughes [16] 1855.	M.	Fish-bone.	None given.	Debility, cough, fetid sputum, night sweats.	.....	.....	Consolidation left apex, later cavity at left apex.	In cavity in left upper lobe.	Died; left lung riddled with gangrenous cavities; right lung normal.
10. Fountain [17] 1859.	M. 10	Chicken-bone.	Swallowed ten days before admission.	Cough, fever; no expectoration.	.....	.....	Dulness and absence of breath and voice sounds below 4th right rib; tenderness.	.....	Recovered; abscess in rt. side opened, later pus evacuated by bowels, 4½ months bone coughed up.

* Case number.

† Bibliography number.

11. Robertet [18] 1864.	M. 8	Piece of umbrella stick.	Six days before admission cough, cyanosis, permanent dyspnœa.	Weak, pain in chest, fever dyspnœa, no fetid odor.	.....	.....	Left chest dull, breath sounds absent, later cavity left apex, friction rub.	Lt. bronchus just above bifurcation.	Died 34 days; left lung gangrenous, no odor; complete obliteration of bronchus (cause or no odor?); pericarditis.
12. Joffe [19] 1866.	M. 41	Cherry-stone.	Swallowed and forgotten.	Pain right side, cough, putrid sputum, fever, chills, sweats.	.....	50 days.	Consolidation right side, tympany lower right front, bubbling rales, left lung clear.	.....	Died; coughed up four days before death; entire right lung, gangrenous; left lung, bronchopneumonia.
13. Barbeu-Dubourg [20] 1866.	F.	Piece of plum-stone	Cough, malaise, pain, frothy sputum.	Cough, pain, fetid expectorations, coughed up fragments.	17 days.	21 days.	Consolidation right back, going on to cavity formation.	.....	Died 38 days; gangrenous cavity in right lower lobe.
14. McGrath [21] 1880.	M. 7	Head of grass.	Fit of coughing, cyanosis at once; quickly subsided; latent one month.	None for one month, then pain right side and back, hacking cough, fever, expectorat'n, first scanty and bloody, then profuse and foul.	10 weeks	2 weeks.	Eight weeks consolidation base right lung, ten to twelve weeks cavity.	In cavity of lung.	Died in 8 weeks; autopsy: lower ⅔ of lower lobe gangrenous: perforation diaphragm, necrosis of liver; involvement of 2 vertebræ.
15. Gresner [22] 1881.	M. 6	Ear of wheat.	Cough: fever on third day.	Cough, fever, pain, fetid expectorat'ns, diarrhœa.	9 days.	.....	Consolidation right upper back.	.....	Recovered; cough'd up foreign body on 160th day; rapid recovery.
16. Vogel [23] 1881, from Gresner.	M 14	Head of grass.	....	Pneumonia, later putrid expectoration lasting one month.	.....	1 month	Cavity.	.....	Recovered after six years; no signs of cavity.
17. Katho [24] 1881, after Gresner.	F. 6	Bone.	.....	Expectorated ten months.	.....	.....	.....	.....	Recovered in ten months.
18. Mader [25] 1884.	M. 37	Bone.	Bone stuck in throat; probang used; dyspnœa and hoarseness relieved.	Chill, pain in right side, fetid sputum.	6 days.	46 days.	Dulness in right back, tubular breathing, later cavity.	Lower branch of right bronchus.	Died 52 days; gangrene right lung, bronchopneumonia left lower lobe.
19. Mackenzie [26] 1889.	M. 28	Collar stud.	No history of swallowing foreign body; suddenly ill.	Third week night sweats, vomiting, chills, fever, putrid expectoration.	.....	13 days.	Consolidation of right back.	In bronchus to right upper lobe.	Died; lower two rt. lobes gangrenous; left lung bronchopneumonia.
20. Monro [27] 1891.	M. 10	Tooth.	Operation under ether for tuberculous knee; tooth probably loosened and aspirated under ether.	Fourth day cough and fever; fourteenth day offensive sputum.	13 days	3 days.	Fourth day rales in left back, seventh day loss of v. f. in left back.	Lt. bronchus.	Entire lung gangrenous and adherent to walls, beginning liquefaction; died 16th day.
21. Burghard [28] 1894.	M. 9	Shoe button.	Swallowed button one month before admission; black in face at onset; cough since.	Cough.	1 month.	.....	Pus at left base, signs of.	Lt. bronchus.	Thoracotomy three times; recovery.

Author.	Sex and age.	Foreign substance.	History.	Symptoms.	Latency of gangrene.	Duration of gangrene.	Signs.	Site of foreign body.	Results.
22. Babes [29]	.....	.....	Two cases mentioned	as having been in his	clinic; no	record	given.		
23. Warrack [30] 1899.	F. 26	Tooth.	Extracted under gas and inhaled.	Four days cyanotic dyspnœa, dry cough; 13th day foul brown sputum.	13 days.	.....	Fourth day left chest immobile at left apex, tub, breathing elsewhere absent over left; thirteenth day friction rub left axilla.	Lt. bronchus above first branch.	Death 16 days; entire left lung gangrenous; rt. lung congestion, œdema beginning consolidation at base.
24. Packard and Le Conte [32] 1902.	M. y'ung	Twig of evergreen.	"Swallowed" foreign body four months previous.	Not given.	4 mos.	... .	Not given.	Not given.	Death 4–5 months; gangrene of lung; twig of evergreen in gangrenous area.
25. St. Philip Nourret.[31]	..... 4 yrs	Ear of wheat.	....	Hemorrhage.	4 days.	6 days	.....	.....	Died 10th day from hemorrhage, gangrene of lung and lymph glands.
26. Schlectandahl[33]	F. 3	Ear of grain 5.5 cm. long.	Whooping-cough several weeks before.	Looked ill, pale, dyspnœa, dry cough, no expectoration, later fetor of breath, including cough; more pain.	?	2½ mos.	Signs of fluid at right back; later discharge and expectoration of foul pus containing necrotic tissue.	Right lower bronchus.	Thoracotomy, later pneumotomy; death in 6 mos.; rt. lung gangrenous, with cavity formation; actinomycosis in pus about f. b.
27. Bugh [34] 1903.	M. 5	Head of wheat.	....	.....	.....	.....	.....	Anterior bronchial branch.	Death from gangrene of lung.
28. Gourment and Andre [35], 1903	M. y'ung	Long pin, glass head.	Pin in trachea; x-ray negative; next day forced downward.	Fever; condition bad.	.....	.....	Signs of bronchopneumonia; second pleurisy; later pseudocavernous.	Head in left bronchus below branch, point in right bronchus.	Death; small focus of gangrene in neighborhood of point of pin.
29. Clarke and Marine.[39]	M. 35	Piece of bone.	Severe cough and hæmoptysis; fever, weakness.	Fever; slow pulse, later foul expectoration.	14 days.	2½ days.	Friction rub and dulness right back, later pneumothorax in front.	Rt. bronchus below first branch.	Death 17 days; gangrene rt. mid. and lower lobes; bronchiectasis; bronchopneumonia lt. lung: actinomycosis in rt. lung.
30. Kisel [36]	Child	.....	Two cases reported in	children; article not	available.				

Over the left lung the breath sounds were loud and harsh, and there were numerous moist rales. On this day an exploratory needle, measuring 8 cm., was inserted in four places in right axilla and right front. The needle just touched the lung when inserted to its extreme limit, and nothing but foul-smelling gas could be obtained from the pleural cavity. During this night the patient sank rapidly, and died at 12 noon on July 17th, the sixth day after admission, or slightly over forty-eight hours after the first appearance of the putrid expectoration. Until the very end the patient continued to expectorate foul sputum, during the last few hours disregarding the receptacle and expectorating upon bed, floor, and walls.

Abstract of Autopsy Protocol. Autopsy performed six hours after death. The body is that of a white, well-built, male subject, 182 cm. long. Rigor mortis is well established, and there is marked postmortem lividity in the dependent parts. The body emits a very fetid odor. The chest is slightly fuller on the right than on the left side. The abdomen is not distended, and on opening it the subcutaneous fat is well preserved. The muscles are very dark red; omentum is normal; the liver extends 13 cm. below the costal margin at tip of ninth rib. The peritoneal surfaces are everywhere smooth and glossy. The diaphragm reaches to the seventh rib on the right side and to the fourth rib on the left. The abdomen is otherwise negative on general inspection.

Chest. On puncturing the right pleural cavity, under water, stinking gas is expelled with considerable force and the liver rises 4 cm. On removing the sternum the right lung is seen to be retracted from the diaphragm about 5 cm., and also slightly from the chest wall over the lower half of the lower right lobe.

Lung. Left: The left lung completely fills the pleural sac, is free from adhesions, and emphysematous bullæ are seen along the anterior margin. There is no excess of fluid, and the surfaces are everywhere smooth and glossy. In color the upper lobe presents a marbled appearance, while the lower lobe is splotchy, dark red. On removal the lung is voluminous, collapses but slightly, and is generally crepitant, but deep in the posterior central portion of lower lobe there are various-sized areas of consolidation, which on section are slightly raised, dark red, moist, and emit a bloody exudate on pressure. The remaining portion of this lung is deeply congested, but crepitant. The pulmonary vessels are clear. The bronchi are intensely congested, dark red, of a foul odor, and their mucosal surface is covered with a bloody, fibrinous exudate, which, when scraped off, takes away the mucosa in places. The bronchial lymph glands are somewhat enlarged, soft, and deeply pigmented. *Right:* The entire upper lobe is bound to the parietal pleura by fibrous adhesions, and the middle and upper portion of the lower lobes by fibrinous adhesions. The lower half of the lower lobe is

retracted uniformly from the parietal pleura and hangs free in the purulent exudate. The pleural cavity contains about 400 c.c. of a greenish-yellow, purulent, foul-smelling fluid.

On removal the lung does not collapse. It weighs 1840 g. The lower and middle lobes present a frosted, dark, grayish-green appearance. All three lobes are adherent to each other. The entire lung is airless, except the apical portion, where crepitant areas are intermingled with lobular consolidation. The lower and middle lobes have a solid, fleshy, slightly fluctuant consistency and flatten out on the table, while the upper lobe preserves its shape.

FIG. 1

Appearance of lung on section (hardened specimen).

On stabbing the lower lobe, for cultures, a dark, grayish-green, thick fluid escapes, which is of an intensely foul odor.

On section, the color of the lower and middle lobes is grayish-green and brown. The cut surface is riddled with cavities, varying in size from a pinhead to a marble. In places it presents a honeycombed appearance, the trabeculæ being the bloodvessels and bronchi, some of which are necrotic and easily broken; the vessels, thrombosed and cord-like, span the areas of liquefaction and produce a multilocular appearance. In places the liquefaction extends quite to the pleura, which is nowhere perforated, but generally

there is a layer of from ½ to 3 cm. of gray-green, consolidated lung tissue surrounding the central area of cavity formations. This tissue is friable, but still preserves its architecture. The lower portion of the upper lobe is solid, dark red, drips blood, and exudation plugs may be expressed from the alveoli. The upper portion is air containing, except for scattered islands of consolidation. On tracing out the branches of the pulmonary artery they are found to be thrombosed as they enter the sphacelated and liquefied areas. From the primary bronchus exudes a thick, dark-red, stringy material. On opening the bronchus a mass is found firmly

FIG. 2

View of internal section showing (1) bifurcation, (2) foreign body in right bronchus (hardened specimen).

lodged in the lower division of the primary bronchus, just below its eparterial branch. On examination of this mass it is found to be a bit of cancellous bone, roughly 1.0 by 0.8 cm., with irregular surfaces. The mucosa at the site of the lodgement presents two small ulcerations. The walls of the bronchus are thinned. There is no evidence of granulation tissue. All the branches of the primary bronchus leading to the middle and the lower lobes are uniformly dilated and filled with the gangrenous liquefaction products. The mucosa is in places necrotic and may be peeled off. Many of the smaller bronchi open directly into the gangrenous cavities. The

primary bronchi and the trachea are dark red, the mucosa sloughing in places, and the entire upper respiratory tract is intensely inflamed.

Heart. With the exception of 100 c.c. clear yellowish fluid in the pericardial cavity, its structures present normal appearances.

Spleen. Dark red, soft, Malpighian bodies enlarged, and weighs 225 g.

Liver, pancreas, kidneys, and *bladder* normal.

Stomach. Walls are of normal thickness; the mucosa shows numerous ecchymoses, and acutely congested streaks radiate toward the pylorus. Mucosa is somewhat thickened, entire, and nowhere softened. The rest of alimentary tract appears normal.

Anatomical Diagnosis. 1. Foreign body (bone) in right primary bronchus, below its eparterial branch. 2. Diffuse gangrene, with liquefaction, of the middle and right lower lobes, and pyopneumothorax. 3. Bronchopneumonia of the right upper and left lower lobes. 4. Acute hemorrhagic bronchitis, tracheitis, laryngitis, and pharyngitis. 5. Acute hemorrhagic gastritis. 6. Acute splenic tumor.

Aërobic tube cultures and plates were made on the ordinary media from the heart's blood and the lungs.

The following organisms were isolated from the gangrenous lung: 1. Streptococcus pyogenes. 2. Bacillus mucosus capsulatus. 3. Proteus vulgaris. 4. A member of the actinomyces group.

Microscopic. Hæmatoxylin and eosin stain. For the sake of brevity we will add only a description of the lung appearances, as the other organs showed only the usual changes incident to acute infection.

The alveolar exudate presents wide variations. Some alveoli contain serous exudate, with varying numbers of red blood cells and a few large alveolar cells containing much black pigment—a hemorrhagic œdema, so to speak. Other alveoli are densely packed with polymorphonuclear leukocytes and fibrin, the strands of which can be seen to extend through the alveolar walls.

The border of a liquefied area shows a granular and necrotic cellular debris bordering on lung tissue, which still preserves its alveolar architecture, though it does not take a nuclear stain, while the exudate stains well. This necrosis of the alveolar walls gradually verges into portions which still stain, though in some areas one observes a slight leukocytic barrier demarcating the alveolar necrosis. In other areas the necrosis is not preceded by hepatization, but has taken place in alveoli filled with serous exudate only. In these areas there is no suggestion of a leukocytic barrier. The bronchi are uniformly dilated and filled with an exudate of leukocytes, red blood cells, granular debris, and elastic tissue, all of which may be demonstrated in the contents of the lung cavities. The mucosa is not to be made out in most places, but is

represented by a dense mass of red blood cells and leukocytes. The submucosa and muscularis are also densely infiltrated. The trachea presents similar appearances.

The bloodvessels are everywhere engorged, and thrombi are seen in most of the smaller vessels as they enter the necrosed areas. The walls of such vessels contain much cellular exudate, and fibrin strands may be seen in the adventitial coat outside of the areas of necrosis. All of such vessels show thrombus formation.

In general the sections give one the impression of a very rapidly progressing gangrene.

The three stages—hepatization, necrosis, and liquefaction—are represented in the space of four alveoli at most, while in many places liquefaction extends quite to the living tissue, with no intermediate zone of necrosis.

The occurrence of gangrene in cases of this kind depends largely on the physical-chemical characteristics of the foreign body, whether hard, soft, smooth, or rough, organic or inorganic. It most frequently follows the aspiration of a rough organic body of moderate consistency. When such a foreign substance becomes lodged in a bronchus, sooner or later certain definite pathological changes may take place. There is more or less initial collapse of the portion of the lung supplied by the bronchus, due to a restricted respiratory interchange and an absorption of the stationary residual air, generally not complete, however, on account of the bronchus not being completely occluded. This permits of a slight interchange of air during respiratory movements, quite sufficient in most cases to allow of some movement of the foreign body, which movement would be more pronounced during paroxysms of coughing, though the tendency is for the mass to become more firmly impacted, due to the difference in the air pressure above and below the mass following the absorption of the stationary residual air, thus producing a suction, so to speak.

The slight mobility, together with the pressure effects incident to the bronchial spasm, produces an ulceration of the bronchial mucosa at the site of impaction, which, infected or becoming infected with the various organisms of the upper tract and inspired air, forms a starting point for the changes in the bronchi, the resistance of which, together with that of the lung parenchyma, is impaired through loss of function. The exudate from the ulceration at the site of impaction, together with the bronchial secretion, gravitates through the bronchial tree and sets up a bronchitis, becoming purulent; later, putrid. The bronchi become uniformly dilated, whether due to the pent-up secretions or weakening of the walls by inflammatory changes[37] would be difficult to say; probably both factors are concerned.

The extension of the inflammatory process through the bronchial walls and to the smaller air passages sets up a diffuse broncho-

pneumonia in the usual way. The involvement of the lung parenchyma spreads more or less rapidly, depending on the virulence of the organism and the resistance offered by the tissues, which is much lowered, for the reasons named above.

That the process is rarely, if ever, a true lobar pneumonia is borne out by the clinical history, the gradual development of the physical signs, and the autopsy findings in the reported cases. As the pneumonic process extends to the pleura, a plastic pleurisy develops, which in some of the cases sharply outlines the amount of primary lung collapse, and which is well shown in our case. Necrosis of the lung parenchyma, which is always diffuse and relative to the distribution and extent of the bronchopneumonia, depends, it would seem, partly on thrombosis of the vessels[38] and partly on a literal drowning of the tissues in septic products. Thrombosis of the vessels appears to be the resultant action of (1) septic products dammed back in the air passages, (2) and of toxins of high virulence on the vessel walls.

Necrosis may follow quickly after hepatization or may be delayed for weeks, but there is evidence to show that the necrosis, when once started, proceeds rapidly, and in places involves tissue even before hepatization has taken place. This condition was noted by Laennec. It indicates a high virulence of the organisms concerned, and a failing resistance on the part of the tissues.

The decomposition and liquefaction of the necrotic areas are brought about partly by autolysis, but mainly by putrefactive and liquefying organisms, producing the foul-smelling products, and in many cases gas.

Pneumothorax may develop either by the gangrenous process extending through the pleura, and producing air communication with pyopneumothorax, or by the gaseous decomposition products collecting in the pleural cavity without actual perforation.

Of the great number and variety of micro-organisms that have been found in association with this condition, the most important and most frequently encountered are the pyogenic group, especially streptococcus, the proteus group, actinomyces group, and various unclassified anaërobes. Without theorizing on the bacterial etiology, most recent authors are inclined to attribute more importance to the anaërobes in the production of liquefaction, and prefer to consider aërobes as playing a secondary part only.

As to the mode of entrance of the organisms, the general opinion is that it takes place from the bronchi, as is suggested by the primary peribronchial occurrence of necrosis and liquefaction, though other possibilities are discussed, especially that *via* lymphatics.[39]

We wish to thank Drs. Edward F. Cushing and W. T. Howard, Jr., for the privilege of reporting this case.

BIBLIOGRAPHY.

1. Laennec. Treatise on Diseases of the Chest, 1819, p. 213.
2. Traube. Ges. Beitr. Bd. ii. p. 405; Reo. Fraenkel (41) p. 538.
3. Gross. Practical Treatment on Foreign Bodies in Air-passages, Philadelphia, 1854.
4. Poulet. A Treatise on Foreign Bodies, etc., Wood's Lib., vol. xxi.
5. Weist. Transactions of the American Surgical Association, 1881, vol. i. p. 117.
6. Hoffmann. Nothnagel's System, Diseases of the Lungs.
7. Murphy. Journal of the American Medical Association, 1898, vol. xxxi. p. 288.
8. Wood, G. B. Philadelphia Monthly Medical Journal, 1899, vol. i. p. 208.
9. Lenglet. Mémoires de l'académie de méd., tome iv. (see 20).
10. Gilroy. Edinburgh Medical and Surgical Journal, 1831, vol. xxxv. p. 293.
11. Lawrence. Bull. Soc. anat., Paris, 1838, tome xiii. p. 162.
12. Brown. British-American Medical and Physical Journal, Montreal, 1850–51, n. s., vol. vi. p. 521.
13. Struthers. Gazette médicale, 1853 (see Barbeu-Dubourg, 20).
14. Hildreth. Boston Medical and Surgical Journal, 1853, vol. xlvii. p. 420.
15. Rothmund. (See 22.)
16. Hughes. Dublin Hospital Gazette, 1855, vol. ii. p. 59.
17. Fountain. North American Medical and Chirurgical Review, 1859.
18. Robertet. Bull. Soc. anat., Paris, 1864, tome xxxix. p. 267.
19. Jaffe. Allg. med. Central. Zeitung, Berl., 1866, Bd. xxxv. p. 233.
20. Barbeu-Dubourg. Paris, Thesis, 1866, p. 29.
21. McGrath. Lancet, London, 1880, vol. ii. p. 89.
22. Gresner. Wien. med. Blatter., 1881, Bd. iv. p 673.
23. Vogel. (See 22.)
24. Katho. Gerhard's Handbuch f. Kinderkrank., Bd. iii. Heft 2, s. 33. (See 22.)
25. Mader. Wien. med. Blatter, 1884, Bd. vii. pp. 101 and 137.
26. Mackenzie. St. Thomas' Hospital Reports, 1889, vol. xix. p. 346.
27. Monro. Transactions Glasgow Pathological and Clinical Society, 1891, vol. iv. p. 194.
28. Burghard. King's College Hospital Report, 1894–95, London, 1896, vol. ii. p. 97.
29. Babes. La Semaine med., 1895.
30. Warrack. British Medical Journal, 1899, vol. i. p. 401.
31. St. Phillips and Nourret. Abs. Centr. f. Chir., 1901, p. 631.
32. Packard and Le Conte. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1902, vol. cxxii. p. 375.
33. Schlechtendahl. Münch. med. Woch., 1902, xlix. p. 449.
34. Bugh. Hoffmann, in Nothnagel's System.
35. Courment and Andre. Lyon méd., 1903, p. 90.
36. Kisel. Diesk. med. Mosk., 1902, vol. vii. p. 64.
37. Sevestre. British Medical Journal, 1899, vol. i. p. 143.
38. Hensel. Deut. Arch. f. klin. Med., 1887, Bd. xli. p. 185.
39. Pauli, F. Inaug. Diss., München, 1902.
40. Dieulafoy. Clinic méd. de l'hotel dieu, Paris, 1901–1902, vol. iv. p. 44.
41. Fraenkel. Spez. Path. und Therap. der Lungenkrankheiten, Berlin and Wien, 1904.

RHYTHMIC LATERAL DISPLACEMENT OF THE HEART AS A SIGN OF UNILATERAL PLEURITIC EXUDATE.

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IN August, 1902, the writer called attention to a rhythmic lateral displacement of the heart, synchronous with respiration, as a sign of unilateral liquid exudate in a pleural cavity. More extended observation has tended to confirm the statements made in that preliminary

report, and has served also to show the value of the sign in differential diagnosis. Opportunities have offered for investigating by means of the fluoroscope and auscultatory percussion combined twenty cases of simple pleurisy with effusion, two of empyema, one of pneumothorax, two of subdiaphragmatic abscess, and two of malignant disease of the lung and pleura, associated with small pleural exudates. Many cases representing the ordinary routine of office and hospital work, embracing a variety of cases of cardiac and pulmonary disease, as well as normal chests, have been carefully examined in relation to the cardiac displacement observable in respiration. Of the miscellaneous cases only one showed any marked lateral movement, this being a dilated heart with mitral lesion and pericardial adhesion. In the cases of malignant disease of the pleura, one sarcomatous and the other carcinomatous, neither showed any marked degree of lateral displacement in respiration. In a case of left-sided subdiaphragmatic abscess from caries the heart was somewhat displaced to the right and upward, but there was no lateral movement in respiration. In the case of pneumothorax the heart was displaced far to the right, the maximum impulse being just within the right nipple line, but no lateral movement of the heart was perceptible in respiration, nor could any movement be expected in such cases, because of the shallow breathing and slight diaphragmatic movement,[1] even of the sound side. All of the cases of simple effusion examined showed the rhythmic lateral displacement in varying but marked degrees, the least movement being observed in a case of massive effusion of the right side, in which instance the heart became very freely movable after the withdrawal of two pints of fluid. In the case of empyema observed the cardiac excursion was like that seen in simple effusions. In all of these cases the heart seems to move upward as well as outward, as might be expected from the nature of its attachment and the forces exerted upon it. An upward and downward movement has long been recognized, and it would seem that this upward movement may have caused observers to overlook the coincident lateral displacement in the presence of a unilateral exudate. The change in the position of the heart is not only to be observed by means of the fluoroscope, but, according to my own experience, is quite readily determined by auscultatory percussion, if not by ordinary percussion, and in some instances of right-sided effusion the lateral shift of the apex beat is evident. In cases of effusion into the right cavity little difficulty is experienced in outlining the left border of the heart by the usual methods.

In left-sided effusions the displacement of the heart and its radius of movement is greater, but auscultatory percussion or the fluoroscope is necessary for the accurate determination of the right border.

[1] The diaphragmatic movement may even be revised—*i. e.*, Kienback's "paradoxical contraction."

In order to secure the deep respirations necessary to the best definition recourse must sometimes be had to the exhibition of morphine. In the course of his work the writer has failed to observe any cases of liquid pleural effusion in which there was no lateral movement of the heart. He has also been unable to confirm the correctness of the observations leading to the statement that in certain cases of this sort the diaphragm is absolutely paralyzed, and in some instances forced downward so as to actually bulge into the peritoneal cavity. Even in a case of massive purulent effusion of long standing the diaphragmatic excursion was marked.

He further ventures to take issue with the statements made by some writers upon the *x*-ray, to the effect that the extent of persistent cardiac dislocation in liquid effusions cannot be accurately determined without the use of the fluoroscope. In nearly every instance of this sort dislocation of the heart to the left was determined without difficulty by ordinary percussion. In the case of displacement to the right auscultatory percussion was found to give results that bore well the test of fluoroscopic examination. In determining the exact extent of the rhythmic excursion of the displaced heart in respiration, however, auscultatory percussion is absolutely necessary in the absence of fluoroscopic examination, because of the lung movement and expansion of the unaffected side. It seems strange that a phenomenon of this kind should escape notice for so long a period, though no stranger, perhaps, than the many instances of a similar sort in the history of medicine.

Indeed, if one considers the forces acting within and about the pleural cavity and the peculiar relation of the heart to the pleural sacs, one cannot avoid the conclusion that movement of that organ from side to side must occur in the presence of a free unilateral liquid exudate, unless the amount of fluid is trifling or the diaphragm paralyzed. In such cases the liquid is in a cavity containing an elastic and compressible lung, and has a powerfully muscular movable floor, acting automatically and by reinforcement in a piston-like manner. The cavity is limited laterally by a chest wall quite rigidly resistant to internal pressure, yet capable of expanding and contracting at will. The amount of force exerted by an effusion is well shown by the prompt and effective compression exerted upon the lung of the affected side, quite apart from the other factors, causing lung shrinkage; and we can readily understand its effect under the law of hydraulics upon the yielding partition represented by the pericardium, its surrounding tissues, and the movable organ inclosed within it. In inspiration the lowered diaphragm and raised ribs enlarge the thoracic cavity; the pericardium is somewhat tautened; the fluid column is lowered and its pressure in part removed; the expanding sound lung exercises opposing pressure. At this time, therefore, the displaced heart tends to move toward the affected side. In expiration the diaphragm rises, the pericardium is relaxed,

the thoracic walls are contracted, the liquid column must ascend, lateral pressure is increased and the movable heart is forced away from the affected side and meets a lessened resistance from the unaffected lung. It would seem to follow that the maximum movement would occur in moderate-sized effusions, and this corresponds to the writer's observations. The following conclusions are offered:

1. A rhythmic lateral movement of the heart occurs in unilateral liquid pleural effusions.
2. Such movement is most marked in medium-sized effusions.
3. The heart approaches the affected side in inspiration and moves outward in expiration.
4. The extent of movement is variable, but often amounts to two inches.
5. It may be measured by fluoroscopic examination, auscultatory percussion, or in the case of right-sided effusions by simple deep percussion of the free cardiac border, or in some instances by mere inspection of the apex beat.
6. Deep breathing and especially forced expiration are essential to the success of the manœuvre, and to obtain this morphine must sometimes be administered.
7. Marked rhythmic lateral movement has not been found in pnuemonia, tuberculous infiltrations of the lung, malignant disease of the pleura or lung, or in subdiaphragmatic abscess.

The writer sincerely hopes that these observations will be fully tested by his colleagues, and that this sign may prove of real value in the differential diagnosis of thoracic diseases.

ORTHOSTATIC ALBUMINURIA.[1]

A CLINICAL STUDY OF A CASE, WITH SPECIAL EXPERIMENTS, SHOWING THE CAUSE OF THE VARIATIONS IN AMOUNT OF ALBUMIN.

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In 1892 a professor of chemistry reported to me that he had employed his own urine in quest of uric acid and was surprised to find that it contained albumin. Upon later examination by myself albumin was found in decided quantities. Repeated examinations developed an unusual case. While the urine was practically normal in quantity and solid constituents, albumin was found to vary greatly in quantity. Numerous cylindroids were present in every specimen examined, but no tube casts.

In order to determine the cause of the albuminuria a systematic study of the urine was begun. For a period of one month tridaily

[1] Reported to the Alumni Association of the Hospital College of Medicine, July 1, 1905.

tests of the urine were made and recorded with other observations made at the same time, while careful note was taken of the varying amount of mental work, exercise, fatigue, etc., of each day.

The method of testing for albumin was to heat the urine in a graduated test tube until it began to boil, allow it to stand for a few moments, add a few drops of dilute nitric acid, and then heat again to the same point. The albumin was then allowed to settle for from ten to twelve hours and its apparent volume read off. The observations were necessarily rough, but they were sufficiently accurate for the purposes intended—to show the daily fluctuation in quantity and the inconstancy.

When the amount of albumin was not sufficient to settle down, but remained as a cloud, it was described as a *cloud*, a *heavy cloud*, or a *light cloud*. If the cloud was scarcely visible it was marked *doubtful*, and if the solution remained clear, *absent*. The figures are used to denote the apparent volume in hundredths—*i. e.*, they denote the *per cent.* by volume.

Observations were made on the amount of albumin: morning (on arising), afternoon (usually about 2 P.M., thus showing the effect of the morning's work), and evening (at bedtime). The evening observation was usually upon urine excreted between 7 and 10.30 P.M. The evenings were usually spent quietly.

The following table records these observations:

Date, 1892.	Morning.			Afternoon.			Evening.			
	Albumin.	Specific gravity.	Temperature.	Albumin, per cent.	Specific gravity.	Temperature.	Albumin, per cent.	Specific gravity.	Temperature.	Quantity in 24 hrs.
Oct. 23	Absent	1.016	97.9°	5	1.023	98.8°	Doubtful	.....	97.6°	
" 24	Doubtful	1.024	97.4	11	1.024	98.5	4	1.025	97.7	
" 25	Light cloud	1.025	97.5	12	1.023	98.3	4	1.025	96.9	
" 26	Doubtful	1.025	97.5	12	1.026	98.9	Light cloud	1.023	97.6	
" 27	Absent	1.025	97.9	12	1.024	98.4	2	1.025	97.3	
" 28	Doubtful	1.026	97.5	3	1.023	98.4	2	1.023	97.0	
" 29	Light cloud	1.030	97.0	5	1.022	98.5	2	1.022	97.8	
" 30	Doubtful	1.028	97.5	2	1.023	.....	8			
" 31	Doubtful	.....	.....	5	.....	.....	Light cloud			
Nov. 1	Absent	.....	.....	14	.....	.....	Heavy clo'd			
" 2	Doubtful	.....	.....	20	.....	.....	2			
" 3	Light cloud	1.026	.....	16	.....	.....	Heavy clo'd			
" 4	Absent	.....	.....	9	.....	.....	Heavy clo'd			
" 5	Doubtful	.....	.....	2	1.024	.....	Absent			
" 6	Absent	.....	.....	Light cloud	.....	.....	4			
" 7	Light cloud	.....	.....	6	.....	.....	Doubtful			c.c.
" 8	Absent	.....	.....	.....	.....	.....	Light cloud	1.026	.....	945
" 9	Absent	.....	.....	5	.....	.....	.....	1.023	.....	999
" 10	Absent	.....	.....	5	1.018	.....	Absent	.....	.....	954
" 11	Absent	.....	.....	3	.....	.....	Absent	.....	.....	1138
" 12	Absent	.....	.....	1	.....	.....	Light cloud	1.024	.....	1070
" 13	Absent	.....	.....	6	.....	.....	Light cloud			
" 14	Absent	.....	.....	5	.....	.....	Light cloud			
" 15	Light cloud	.....	.....	4	.....	.....	Light cloud			
" 16	Absent	.....	.....	4	.....	.....	Heavy clo'd			
" 17	Doubtful	.....	.....	Heavy cloud	.....	.....	Light cloud			
" 18	Doubtful	.....	.....	Light cloud	.....	.....	Doubtful			
" 19	Absent	.....	.....	Doubtful	.....	.....	Light cloud			
" 20	Absent	.....	.....	.....	.....	98.4	Absent	.....	97.4	

The reaction of the urine was taken three times a day for one week, and always found to be acid, but was afterward found on three occasions not sufficiently acid to keep all the phosphates in solution.

The quantity of urine as shown in the above table was found to be *diminished*. On the days (November 11th and 12th) on which the quantity was increased to 1138 c.c. and 1070 c.c. more liquid than usual was drunk in order to test its influence upon the quantity of urine. The urine in all subsequent examinations has been found deficient in quantity, and the specific gravity, as at first, rather higher than normal. The temperature recorded in the table was taken under the tongue. The urine was free from sugar.

It is not possible to state the amount of physical work done during each day that the observations were made, but it was found, as the table partly shows, that, as a rule, the greater the amount done the greater the amount of albumin. Perhaps it is better stated by saying the amount of albumin varied directly as the amount of *fatigue* felt. Days when the general physical condition was below average were days of increased albumin if the amount of exertion remained the same.

Although fatigue seemed to favor the passage of albumin in increased quantities, it appeared to be a contributory rather than an exciting factor.

As shown by a study of the patient's daily habits in connection with the tests, the exciting factors appeared to be either the erect position or the mental and nervous strain incident to teaching.

Both of these factors were absent during the sleeping hours, and the morning urine was invariably either free or almost free from albumin. Both factors were present in the forenoon, all class work being done then, and the duties of the work necessitated being on the feet the greater part of the time, and at this time albumin was more abundant than at any other time. The days upon which no work was done, the forenoon being spent quietly, the afternoon urine contained decidedly less albumin. In afternoons no teaching was done and very little mental work was indulged in, and therefore nervous and mental strain could be eliminated as a factor bearing upon the variations in quantity of albumin found in the evening urine. In direct proportion to the extent of time spent in standing or walking—that is, in the upright position—was the amount of albumin.

In order to show more clearly that the erect position was the exciting factor, and that the case was one of orthostatic albuminuria, the following special experiments were made. In these experiments the following method was carried out: The bladder was first emptied and the urine found to contain no albumin or only a trace. The urine secreted during the experiment was obtained, while that passed immediately after the experiment was usually discarded,

and when the conditions which preceded the experiment had been renewed a short time the urine was again tested.

EXPERIMENT 1. Standing nearly still and quite unsupported. At the end of the first fifteen minutes, 40 per cent. by volume, albumin; at the end of the second fifteen minutes, 30 per cent. by volume, albumin; at the end of the third fifteen minutes, 33 per cent. by volume, albumin. Albumin was *absent* at the beginning and disappeared entirely on sitting still half an hour.

EXPERIMENT 2. Standing *quite* still on two feet for five minutes and then sitting down for ten minutes gave albumin 12 per cent.

EXPERIMENT 3. Same as experiment 2, gave 45 per cent. albumin.

EXPERIMENT 4. Same as experiment 2, but standing on one foot, gave 20 per cent. albumin.

EXPERIMENT 5. Standing quite still on both feet for fifteen minutes gave 70 per cent. of albumin, the largest amount observed in any of the experiments.

EXPERIMENT 6. Kneeling erect, supported only on knees and toes, gave 65 per cent. of albumin.

EXPERIMENT 7. Sitting very erect on a narrow seat for fifteen minutes was without distinct effect.

EXPERIMENT 8. Standing in such a way that the back was pressing against a wall and the knees were pressing against a board in front, while the arms were resting on another board in front, relieving to some extent the strain on the back, produced after remaining in this position fifteen minutes no effect upon the secretion of albumin.

EXPERIMENT 9. Walking quickly fifteen minutes gave albumin 8 per cent.

EXPERIMENT 10. Same as experiment 9, gave albumin 25 per cent.

EXPERIMENT 11. Walking for an hour leisurely gave only a trace of albumin.

These experiments were not performed in the order given, and each was performed on a different day. In all albumin was absent in the beginning, and either absent or in traces half an hour after the experiment.

The following experiments were without apparent effect on the amount of albumin: Overeating, eating too little, taking a small dose of brandy, mental excitement (including sexual), and mental depression; *any kind of exercise in a horizontal position*, even when the lower part of the back was left unsupported for some time, the body resting on the head and upper part of the back and on the legs below the knees.

The urine in this case at no time contained an abundant sediment. It was usually clear, occasionally cloudy on standing from precipitation of phosphates, and of a normal, straw-yellow color.

The microscope revealed abundant *cylindroids* at every examination, but repeated and careful examinations failed to reveal hyaline or other tube casts. In July, 1893, nearly one year after these examinations, the patient consulted Dr. William Osler, of Johns Hopkins University, who also found cylindroids in abundance but no tube casts.

On May 26, 1893, seven months after the first observations were made, and just previous to his return to his home in Canada, the last systematic examination of his urine was made. It showed the quantity in twenty-four hours to be 860 c.c.; color, straw yellow; specific gravity, 1.025; albumin, 3 per cent. by volume; urea (Liebig's method), 3 per cent. by volume, and cylindroids. There was very little physical or mental exertion on the day of the passage of this specimen.

These special experiments seem to show quite conclusively the erect position to be the cause of the passage of albumin, and consequently that this is an orthostatic albuminuria. In the opinion of the patient, whose training and methods of observation make his opinion of consequence, the experiments seemed to show that the immediate cause of the passage of albumin was *not* simply the erect position or the putting of a strain upon the muscles of the back and thighs, but that it was due to that particular strain which is produced when the body is being held erect; that is, the strain resulting from the act of balancing.

The subject of the observations just described was a college professor and chemist, born and reared in Canada. He was twenty-six years of age, and unmarried when the albuminuria was first detected.

He married two months later without my approval, and in the twelve years of his married life has remained childless. His weight was only one hundred and twenty-eight pounds, decidedly below the normal, his height being six feet one inch. His build, however, is a family characteristic, which may partly account for his light weight. In appearance he was thin, pale, and sallow. Apparently sick, he insisted that he felt perfectly well. He had energy, a good appetite, slept well, and other than the albuminuria, had, as he expressed it, "absolutely no symptoms." He was, however, languid, irritable, and often mentally depressed. Physical examination revealed no abnormality of any organ, except this presence of albumin in the urine, and possibly a very slight accentuation of the second cardiac sound and a distinct though not decided increase in pulse tension.

His family history was excellent. His habits were at this time, and had always been, good. He had never used tobacco nor alcohol. Thus nothing in his family history nor in his mode of living could be ascribed as the predisposing cause of the albuminuria. He had never had scarlet fever nor diphtheria nor any other serious illness

in his recollection. His only illnesses since grown were an acute affection of the lungs in 1886, and a severe attack of tonsillitis in 1889; the former confining him to the house six weeks, the latter accompanied by high fever, confining him to bed for four days. These two illnesses appear to be the only incidents in his history which might bear upon the cause of the albuminuria. The nature of the albuminuria, however, suggests that it did not have its origin in an acute nephritis. It seems probable that his peculiar build, suggesting a loosely built tissue structure, his anæmic condition, and his nervous temperament are etiological factors.

No change in the character of the albuminuria took place during the two years succeeding its detection. The albumin appeared daily and the cylindroids continued numerous, but no tube casts could be detected by either Dr. Osler or myself.

After the second year, the patient having removed to his old home in Canada, I could make no further tests of his urine, and not until a few weeks ago, over twelve years after the albuminuria was first noted, was I able to procure a specimen of his urine for examination. This specimen showed that the nature of the case had changed. It was now found to have the following characters:

Quantity in twenty-four hours, 800 c.c. (27 ounces); color, deep yellow; reaction, acid; specific gravity, 1.025; urea (and uric acid), 4.41 per cent.; albumin, small quantity (about 1 per cent. by volume); sugar, none; tube casts, granular and hyaline, a few; squamous and small round epithelial cells, and amorphous phosphates. The patient reports that his health is probably better now than it was twelve years ago. He states that he has been actively engaged as experimentalist on a government farm in Canada, and that he has not been incapacitated from business by sickness since the detection of albumin twelve years ago. He has no œdema, no cardiac asthma, nor any other constitutional symptoms of albuminuria. He, however, admits that his appetite is small, and that he now eats five meals a day in order to avoid a headache, which usually comes on three or four hours after the last meal when only three are taken. He contends that there is not now any increase in arterial tension.

This case is of especial interest because of the unusual points in diagnosis involved. In the early stages of the disease—that is, for the first two or more years—the orthostatic albuminuria in which the quantity of albumin was often very large, the quantity and density of urine normal, numerous cylindroids, no tube casts, and no constitutional disturbance presented an exceptional clinical picture. It is a group of symptoms which does not include tube casts, polyuria, and deficient elimination, the most characteristic symptoms of an early chronic interstitial nephritis—the only form of nephritis that would be likely to extend over a period of more than twelve years.

Neither is such a group of symptoms usual in a so-called functional albuminuria, because the albumin often appears in large quantity, and the albuminuria has persisted for many years.

After an interval of more than twelve years, during which the albuminuria presumably continued, the symptom group was found to have changed. The urine was decreased in quantity and increased in density (the per cent. of urea and phosphates was above the normal). Tube casts were found, but cylindroids were absent. No œdema, no circulatory nor constitutional disturbance. This group of symptoms is also exceptional.

That a nephritis now exists is shown by the presence of tube casts. But contrary to the usual course of a nephritis, polyuria has never been present; renal elimination is practically normal, and general health is in no way impaired, a though the albuminuria has been present twelve or more years.

These unusual groups of symptoms appear to indicate that the albuminuria began and continued for an indefinite period (more than two years) without the existence of renal inflammation or organic lesions, but that the long-continued irritation incident to the disordered condition, giving rise to the albuminuria, finally resulted in a nephritis.

That renal elimination and circulatory equilibrium have not been impaired at this late period is indicative that but one kidney is involved in the diseased process, and that these functions are maintained by the healthy kidney. The absence of pathological changes in the kidneys for at least the first two years is suggested by the absence of tube casts and the orthostatic form of the albuminuria. This view would also be supported by the unimpaired elimination and good health as late in the disease as the twelfth year if evidence that but one kidney is involved was wanting.

Many authorities support the view that a renal albuminuria can exist without the pathological lesions of the kidney being present.

Herringham[1] attributes pressure on the renal veins as the cause in a case of cyclic albuminuria, in which the albumin passed only during maintenance of the erect position.

Heubner[2] considers orthostatic albuminuria as an expression of general weakness not associated with any renal structural change.

Broadbent[3] finds as an antecedent to "postural" albuminuria a neurotic family history and cardiovascular irritability or brain abscess. He has never seen any serious renal disease result from it. He advises for treatment simple food, fresh air, and vigorous exercise, and asserts that if these cases are treated for renal disease they will probably get worse.

West[4] forms the conclusion that functional albuminuria is always pathologic, though not necessarily renal.

The primary causes of the albuminuria in this case appear to have been a loosely built renal structure[5] and an anæmic condition,

which seemed to act as predisposing factors, causing the passage of albumin only when augmented by pressure upon the renal veins resulting from the erect position. A loosely built renal structure is suggested by the general build of the patient.

As the significance of cylindroids still remains in doubt, the diagnosis in this case must be made without the aid the cylindroids would probably give if they could be properly interpreted. Their presence simply served as an evidence that the albumin came from the kidneys, and their disappearance with the appearance of the tube casts served to show the condition of the kidneys had undergone a change.

No mention is made in this report of treatment because no systematic treatment was instituted. Tincture of chloride of iron was taken for one or two weeks soon after the albuminuria was detected, and aside from the maintenance of proper hygienic measures no other treatment was followed.

REFERENCES.

1. W. P. Herringham. British Medical Journal, 1891, vol. i. p. 219.
2. O. Heubner. Henoch Festschrift, 1890, p. 170.
3. Broadbent. Journal of the American Medical Association, January, 1904, p. 278.
4. West. Ibid., February, 1904, p. 409.
5. Hingston Fox. Lancet, December 12, 1892, suggests as a cause of cyclic albuminuria a loosely built circulatory apparatus.

ASPIRATION IN ACUTE ARTICULAR RHEUMATISM.

BY F. J. B. CORDEIRO, M.D.,
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OSLER has this to say of acute articular rheumatism: "Rheumatic fever, as Newsholme has shown, occurs in epidemics without regular periodicity, recurring at intervals of three, four, or six years, and varying much in intensity. A severe epidemic is apt to be followed by two or three mild outbreaks. The curves of the mortality statistics approximate very closely to those of pyemia, puerperal fever, and erysipelas, diseases which are certainly associated with specific micro-organisms (Church). Physicians have long been impressed with the striking similarity of the symptoms of rheumatic fever to those of septic infection. In the character of the fever, the mode of involvement of the joints, the tendency to relapse, the sweats, the anæmia, the leukocytosis, and, above all, the great liability to endocarditis and involvement of the serous membranes, acute rheumatic fever resembles very closely pyemia, and may, indeed, be taken as the very type of an acute infection. But, as Stephen McKenzie remarks, acute rheumatism should be con-

sidered not simply from the point of view of the rheumatic polyarthritis of the adult, but as a whole in its manifestations at different periods of life; yet even from this standpoint the multiform manifestations of the rheumatic poison in childhood and young adults may very reasonably be referred to the effect of the toxins of micro-organisms.

"The bacteriology of acute rheumatism has lately attracted a great deal of attention. Mantle, Sahli, Leyden, Chvostek, Singer, Achalme, and others have contributed important studies. A review of their work, however, justifies the conclusion that no positive proof has as yet been offered of the constant association of any special micro-organism with the disease. Singer, in an extensive monograph, attempts to show that in rheumatic fever the organisms, consisting chiefly of staphylococci and streptococci, are discharged in numbers in the urine."

And he further says: "Medicines have little or no control over the duration or course of the disease, which, like all other self-limited diseases, practically takes its own time to disappear. Salicylic compounds, which were regarded so long as specific, are now known to act chiefly by relieving pain. R. P. Howard's elaborate analysis shows that they do not influence the duration of the disease. Nor do they prevent the occurrence of cardiac complications, while under their use relapses are considerably more frequent than in any other method of treatment."

Strümpell says: "Acute articular rheumatism is an infectious disease. This is shown by all its clinical and anatomical characteristics, and although we are not yet definitely acquainted with the specific organized poison which gives rise to it, still it is impossible to come to a correct understanding of the symptoms and course of the disease, unless we assume that it is caused by an infectious germ. Of precisely what variety the special germ of acute rheumatism may be, we do not yet know. Still, many recent investigations (Sahli and others) seem to prove that at least in many cases the chief role is played by the staphylococcus pyogenes. In that case we would have to regard it merely as a special clinical form of staphylococcus infection and place it among the mild varieties of septic infection. Indeed, upon more careful consideration, this conception of articular rheumatism seems very probable."

For some years it has been my custom to regard and treat acute rheumatism as a surgical and not as a medical disease. It seems to me that the work of the elder Flint years ago was in the nature of a strict demonstration. This investigator compared by series the results of the different methods of drugging of his time with a control series of patients with absolutely no treatment except palliatives for pain. The result was that the untreated cases did fully as well if not better than those which had received the various approved antirheumatics.

Early in 1899 I reported a typical case of acute rheumatism treated by joint aspiration and nothing else. The disease had shifted around the various larger joints until it attacked the right knee with particular violence. The accumulation of fluid in the joint was so great as of itself to semiflex the leg. Any attempt to straighten the leg caused excruciating agony. The skin over the joint had the familiar erythematous blush and was manifestly hotter than the neighboring skin. The distention was so great that the capsule absolutely seemed to be thinned and the fluid could be felt not more than a quarter of an inch away. Everything demanded the evacuation of this fluid, and accordingly the joint was completely aspirated with the following result. We may here remark that the introduction of the aspirating needle causes very little pain and can be made practically painless by the use of cocaine. The leg after aspiration was straightened out with a feeling of comfort. Even rough manipulation of the joint caused no pain. The erythematous blush of the skin disappeared. The joint was no longer hotter than the surrounding parts. The temperature immediately fell from 102° to 100°. The remaining temperature was in all probability due to the other joints which were moderately implicated. The disease after this shifted to various joints, but the accumulation of fluid in them seemed too small to require aspiration. The aspirated knee was not again attacked and the duration of the illness was ten days. Since then it has been my routine practice to aspirate a joint where there is fluid enough to warrant it.

The following case illustrates well this method of treatment: A. W. B., a fireman, whose work necessitates his staying in a torrid atmosphere, where he is constantly dripping with sweat. He is in the habit of coming out into the open air occasionally and cooling off suddenly. His first attack was on May 29, 1905, and he was treated by his medical attendant in the routine way. Right ankle and left knee were first attacked and then various other joints. Temperature varied from 101° to normal. Treatment consisted of salicylate of sodium, bicarbonate of sodium, and oil of gaultheria, and tincture of iron. Was able to return to his work June 18th, the duration of his illness being twenty days.

He had a recurrence on June 26th. At this time his knees and wrists were involved and his temperature was 103°. On June 29th a note says: "Right ankle, knee, and wrist swollen. Pain in left elbow and knee. Patient very sick last night. Unable to sleep and suffered much pain."

I saw the patient June 30th and aspirated 2 ounces of fluid from the right knee, which was the joint principally affected. The temperature remained normal after this, and on July 2d he was walking about. Resumed his work July 4th.

On July 21st he came on the sick list again with a slight recur-

rence. Right wrist and shoulder-joints and elbows swollen and painful. Temperature did not go above 100°. He was treated by his medical attendant in the routine way and resumed work on July 24th.

On August 5th the patient had another relapse. Temperature 100°. Right ankle distended with fluid. This ankle was immediately aspirated, and on the following day some remaining fluid was withdrawn. Patient made practically an immediate recovery and resumed his work on August 10th.

On August 16th, after remaining perfectly well between times, the patient had still another attack. He presented himself with a temperature of 100.4° and left knee distended and painful. Joint was immediately aspirated, and he made a quick recovery, going to work again on August 20th.

The attacks of August 5th and August 16th did not necessitate his going to bed. After the aspiration in each case he was able to walk without much pain.

The number of my cases is too few to draw any general conclusions, but the fact is noted that in these few cases an aspirated joint has never been reattacked during the same or a subsequent illness. Whether this will continue to be the case or not a larger number of observations must decide.

Recently Dr. O'Conor, of Buenos Ayres, regarding acute rheumatism as a septic infection, has freely opened and drained all affected joints. A report of one of his cases states that : "Both knee-joints were opened, irrigated with normal salt solution under aseptic conditions, and a rubber drainage tube was inserted. Both ankles were incised in three places, the joints opened, and gauze drainage inserted. All medical treatment was discontinued. The knee-joints were washed out daily after the operation. On the third day after the operation the man was able to move all the joints operated upon. On the fifth day after the operation the drainage was removed from the knees. Operation was performed April 23d. On May 29th his joints were all in excellent shape and his general health good. On June 5th he was readmitted with slight fever and some pain, practically all muscular. His joints and muscles were massaged and he was given sodium salicylate. His general appearance was excellent."

Such radical measures are, I believe, entirely unnecessary, everything that can be accomplished by them being attained in a much simpler and more satisfactory manner by aspiration. An aspirated joint makes a practically immediate recovery, while an operated joint requires weeks for the wounds to heal.

In the bacteriology of acute rheumatism I am unable to find that the joint fluid has ever been directly examined for the specific micro-organism, though it would seem somewhat improbable that such is the case. With no intention of entering into the bacteriology

of this disease, I would merely state that the fluid in the case reported above was examined with the following result:

A number of bodies which seemed to be zoöglear masses were observed and these were crowded with extremely minute round bodies, micrococci or spores. These bodies did not stain readily, at least a two-minute immersion in the aniline dye did not alter their appearance. Possibly the micrococci were protected by their gelatinous envelope or the bodies were spores, and for this reason refractory. A single observation in such matters is not of much value, but it would seem that if the specific micro-organism is eventually found it will be in the joint fluid.

THE RATIONALE OF THE ROENTGEN RAY.[1]

By James W. Hunter, Jr., M.A., M.D.,
of Norfolk, Va.

The oft-repeated statement that "the use of *x*-ray in the treatment of malignant tumors is wholly empirical" is so absolutely contrary to the mass of observations that have been collected, and so totally out of harmony with general experience, as to call forth an emphatic denial. True, no reason can be assigned for many facts observed; indeed, we cannot explain why any cause produces an effect. No one will refuse to believe that the burning of hydrogen in an atmosphere of oxygen results in the formation of water. Yet he will not call this empirical; nor can the *x*-ray be called an empirical agent. It is the purpose of my paper to prove this assertion. I have, it is true, some theories to offer. These are based upon my own experience, and, I believe, will explain many things in a satisfactory manner.

If the normal skin be exposed to the action of strong sunlight, as in the case of a bather, there will develop a redness and often a tanning. A blistering results if one remains exposed for a sufficient time; in other words, an inflammation. But it is also true that the body area protected by the thin bathing suit is not nearly so much affected. Similarly let us expose our patient to the *x*-ray. After a sufficient exposure, dependent upon the quality of the ray employed, there will develop a slight erythema, a pronounced redness, or even a blistering. If the reaction be carried far enough an actual destruction of the skin results. Thus we may have the rubefacient action as of turpentine, the blistering of cantharides, or the absolute destruction of the actual cautery.

But the employment of these agencies produces no results other than those of an inflammatory character; there is no selective action. To understand this we must accept the law of Miller. There is no

[1] Read before the Medical Society of Virginia, October 25 1905.

tissue in a malignant growth which has not at some time been present in the body. Indeed, the theory of Cohnheim, which is now the best that we have, defines a malignant growth as a mass of embryonic tissue arising from a focus of congenital or postnatal origin. When it is remembered that the nine months' intrauterine life of the individual develops from a fertilized ovum of about $\frac{1}{100}$ of an inch in diameter a baby of seven and one-half pounds, is it surprising that some carcinomata and sarcomata develop so rapidly? But this very rapidity of growth, as well as a greater complexity of cell structure, tends to a weakened resistance. If now we can summon any agent that, in destroying the malignant tissue, will leave untouched the good, we have indeed a boon. This is precisely what the *x*-ray does.

The excellent work of Scholtz, quoted by Pusey[1] and Caldwell, as well as that by Pusey himself, and the still later studies of Vose[2] and Howe, have shown that the changes following the exposure of epitheliomata to the ray are precisely those of an inflammation. There is a dissolution of the malignant cell, a disappearance, and a replacement by scar tissue. In the case of rodent ulcers the epithelium growing over the scar tissue restores the integrity of the skin. The tissue changes are thus those of substitution, a non-malignant for a malignant growth. But, these same tissue changes go on in the cell, not in the connecting substance—a paralyzing, a killing of the less resistant structures, and a replacement by a non-offensive tissue. And it should be remembered that, as all poisons stimulate when given in small quantities, so with the *x*-ray. Sufficient dosage must be given, else our very object be defeated.

That discouraging reports have been received regarding the treatment of the deep carcinomata or of the epitheliomata of the mucous membranes must be confessed. To quote a recent editorial[3] in the *Journal of the American Medical Association:* "At the present time we have little evidence that the *x*-ray has any real value in the treatment of internal cancer. It is true that we have reports of recessions, of arrest of growth, even of symptomatic cures of internal cancers during treatment with *x*-ray, but we have as yet no reports of absolute cures that can withstand criticism." What is the explanation? My own ideas are these: first, that the rays, having to pass through large amounts of tissue, are thus deprived of their full power; second, that as the rapidity of a malignant growth is largely determined by the resistance of the surrounding tissue, so the curability of any growth or disease is inversely proportionate to its deviation from the normal. Let us consider these propositions in detail.

It has long been observed that in the case of the sunburned bather that part of the skin covered by the suit is less burned than the arms, legs, or neck not so protected. The same thing is noted in regard to the *x*-ray. Williams[4] pertinently inquires "why a few layers of

gauze, the resistance of which to the ray is hardly perceptible on the fluoroscopic screen, should diminish so markedly the effect upon the skin and also the bactericidal effect." There is thus an absorption of the *x*-ray, as well as of sunlight. Now if this occurs in the case of a few layers of gauze, and the full therapeutical effect be prevented, what can we expect in a deep growth? True, we shall use a ray of high penetrating power, yet the fact remains that, after passing through so much skin and other tissue, so little of the original ray remains as to be but feebly effective. Increase the amount and the penetration, you say. Do so and you will only cause a destruction of the superficial structure and do your patient much harm. Interpose a screen, so as to get rid of the lesser rays. You only add to the amount of tissue to be penetrated.

The rapidity of a malignant growth is largely determined by the resistance of the surrounding tissues. Not entirely, for the type is by far the greater factor in its increase; but, since the surrounding tissues are invaded, it is manifest that, other things being equal, the less the resistance the greater the invasion. This is particularly true in certain epitheliomata. The resistance of the surrounding skin causes a compression of the tumor, with the resulting whorls. So much so, that the more the whorls, the more benign the growth. Now this is exactly what occurs in the treatment of the neoplasm or other disease. Some epitheliomata will begin to diminish by the fourth or fifth exposure; not so with lupus or acne. These being bacterial diseases, and of a nearer approach to the skin, must be treated until a severe dermatitis results. But in the case of breast or uterine carcinomata there is little or no resisting media. On the contrary, there are large amounts of glandular tissue of one kind or another, admirably serving to disseminate the disease to the uttermost parts of the body.

As regards the growths on mucous surfaces the same holds true. There is too little resistance; the various secretions with which they are covered keep them soft and moist. In the attempt to cause a breaking down of the malignant tissue we also destroy the surrounding cells. Sometimes, however, some good may be done, as the following case will show:

Mrs. K. (referred to me by Dr. E. E. Field). Widow aged seventy-four years. No children. Eighteen months before had noticed a pimple on inner surface of greater labium (vaginæ) on right side. This had gradually enlarged and broken down, causing a considerable pain on micturition. Sixteen exposures, varying from five to fifteen minutes, were given from December 30, 1904, to January 23, 1905, with the production of a severe dermatitis and some blistering. By February 15th, however, the dermatitis had, under a soothing ointment, entirely subsided, with the complete healing of the denuded area. The cancerous patch showed as healthy a scar as I have ever seen. Symptomatically the patient was cured.

On April 10th I was again consulted and noted a recurrence around the clitoris, involving the lesser labia. I advised another course of the *x*-ray, but to this the patient would not consent. During my absence from the city three days later another physician was consulted. Thus the case passed out of my hands. Her subsequent history is about as follows: Her new physician thought best to cauterize the growth. For this he was dismissed. Toward the end of May she removed to a neighboring city, where the growth was excised. General carcinomatosis ensued, and she gradually sank until early in September, 1905, when she died.

I do not believe that a cure could have been accomplished, owing to the patient's age and the course that these cases invariably pursue. My own experience agrees with Dittrick's,[5] but I do believe that a second course of the *x*-ray would have been of marked benefit, and that the subsequent operation only hastened the patient's death.

We know that those tissues arising from the epiblast yield best to the *x*-ray, and of these chiefly the skin. The accessibility of such growths, as well as the resistance of the surrounding tissues, make epitheliomata the most favorable class for treatment; more especially is this true of the rodent ulcer type. Yet it were folly to maintain that no permanent or even palliative good can be rendered patients affected with other ills. Certain it is, however, that much work must be done ere the final word be spoken. In this respect I wish to give my experience with a most interesting case.

Miss H. H. (referred to me by Dr. H. M. Nash), aged seventy-three years. Father died of consumption at twenty-seven; mother died of pneumonia at eighty-four; half-sister died of consumption at thirty-six; another half-sister died at twenty-eight of uterine complications; a sister died in childhood. Usual diseases of childhood. Used to suffer with dysmenorrhœa; menopause about forty; other history negative.

First seen May 2, 1905. Patient stated that eighteen months before a boil had occurred in the right axilla. This had broken, but gradually there had been an involvement of the right breast, elbow, and supraclavicular space. Some of these had ruptured; that on the neck had been incised, yet the spreading continued. When I first saw her there was a large red tumor about the size of an orange occupying the supraclavicular space and discharging a thick creamy exudate, an enlargement and drooping of the right breast, a sinus in the right axilla, a large mass of glandular tissue at the inner and upper aspect of the right arm, and an involvement of the whole surface above and below the elbow. No other lesions were found; splenic examination negative; patient very thin. Blood: reds, 3,500,000; whites, 24,000; hæmoglobin, 75 per cent.

A diagnosis of Hodgkin's disease was made, which diagnosis was confirmed by Drs. Nash and Grandy.

Some thirty-three exposures, varying from five to ten minutes, were given between May 2d and July 13th, with the production of an erythema on the breast and inner arm, and the disappearance, save for some scabs, of the supraclavicular tumor. Just after beginning treatment a slight metastasis formed over the thyroid. This also discharged and vanished.

On August 1st the condition was about as follows: Breast almost normal; congested milk glands still to be felt. Tumor of neck gone, save for some scabbing, though a slight discharge still continues. Tumor on inner aspect of arm (originally about four inches by three inches by two inches) reduced to about one-third of its original size.

Slight metastasis on back (from neck) and large tumor on outer aspect of right arm, measuring about six inches by four inches by three inches.

From August 1st to this writing (October 14th) some thirty-one exposures have been given with this result. Breast normal in appearance and on palpation; supraclavicular involvement gone, save for a few scabs and one small lump; no discharge. Metastasis on back much smaller. A coalescence of tumors on upper arm with great reduction, measuring about three inches by three inches by two inches. Arm normal size; elbow involvement still greatly enlarged, but some reduction.

The case is still under treatment, and will be reported in detail.

Let us now examine the clinical manifestations appearing during a course of *x*-ray treatment. We shall take an epithelioma. After the fourth or fifth exposure a diminution in size may be noticed, and this diminution continues until a severe dermatitis is obtained. Scab after scab forms, only to be cast off, a heavy and permanent one finally occurring. Healing gradually takes place under this, when it too is cast away. But what has become of the malignant cells? These have discharged outwardly, causing a considerable running, or there has been an absorption. The toxic material, acting as a general poison, causes all sorts of malaise, nausea, vertigo, headache, etc.; so much so that its continuance will put the patient in bed.

Thus the removal of the offending material occurs through an ulceration or a phagocytosis.

With the bacterial diseases a different course ensues. In lupus vulgaris there is an apparent change for the worse. We thus produce a moderate dermatitis with its scabbing and wait until the inflammation subsides. Healing then occurs. In acne, on the other hand, there seems to be an abortive effect; the pustules dry up. Others occur from time to time, but after the production of a derma-

titis once or twice a permanent cure is generally effected. Thus from a clinical, as from a histological standpoint, the *x*-ray is proved to be a destructive agent.

What then is the *x*-ray? We have seen its clinical and histological results; by virtue of what properties does it produce them? To accomplish any result we must have at least two factors: first, the agent; second, the substance acted upon. To give just one example, sulphuric acid of itself can do nothing. Let it come in contact with zinc, and we have a violent chemical reaction. Thus we have the *x*-ray as one factor and the tissues of our patient as the other.

The *x*-ray is quite correctly placed in the class of light. It follows the general law of light, its intensity varying inversely, as the square of the distance, yet it can neither be reflected nor refracted. Even though the rays be passed through a fluorescent substance (such as the double cyanide of bar ium and platinum or tungstate of calcium), there is no bending. Again the ray influences the photographic plate as truly as sunlight. But just what part of the spectrum it occupies is still doubtful, though as the photographic plate is not affected by rays below the red, and our own eyes can appreciate nothing beyond the violet, it is supposed that the *x*-ray lies somewhere beyond the violet. Since the waves of ordinary light become shorter as we approach the violet, it may be that in the *x*-ray we have an exceedingly short wave, or more probably only a series of impulses in straight lines. However, for our purpose, the ray must be considered as an agent on account of its properties as light. But this is not all. Were it so, the *x*-ray would be of no advantage over the Finsen light; that acts purely by reason of its light. It lacks, however, the penetrating quality of the *x*-ray; and this very factor seems to me to explain why lupus and its kindred diseases yield so much more quickly to the *x*-ray.

We may recall that AgCl or AgI is, under the influence of lights above the red, split into its component parts, metallic silver being deposited upon the plate with the libration of chlorine or iodine. Now, if the *x*-ray likewise causes this reaction, is it not also capable of disassociating the various substances that make-up the highly complex embryonic cell? This factor, it seems to me, has been greatly overlooked. We have seen that certain substances will cause a fluorescence; the same thing is true of the tissues. Light taken in as one quality is stored up and emitted as another. Morton,[6] therefore, strongly advocates the administration of fluorescent substances, particularly quinine or fluorescin. With neither of these have I had any experience; personally I never administer quinine except for an urgent cause. I have, however, used the cacodylate of sodium as suggested by Pusey, and can testify that a much quicker result is obtained by its administration; another

proof, it seems to me, that the fluorescent quality of our tissues is largely responsible for the results accomplished.

The *x*-ray must not be considered as a "cure-all." Some things it cannot do; in some diseases there is no improvement over the older treatment; in its own proper sphere it is almost all powerful. That it will ever succeed the usual surgical methods in the treatment of malignant disease is hardly probable. The combination of the two—first, removal, and, second, exposures to the ray—should, however, greatly increase the percentage of cures. In small growths the *x*-ray should be given the preference, as it leaves excellent scars, and is attended by perhaps less recurrences than surgical procedures. In the late stages of malignant disease, or in recurrences after the removal of the breast, the *x*-ray may be the means of prolonging life, as further surgical interference is useless. Pusey comments that his results in these cases have been so unexpected that he never declines them. For my own part, I believe that every hope should be extended our patients. My meaning will best be illustrated by this case.

Mr. S. (referred to me by Dr. H. N. Nash), aged sixty-seven years; married. Eight children; three dead. Lupus vulgaris, including entire nose, for about twenty-two years; kept down by applications of the acid nitrate of mercury. Six months prior to consulting me (March 13th) there has developed in addition an ugly ulcer on the right cheek. Toward its upper aspect there was a growth with the characteristic cauliflower appearance. The surface involvement was about two inches by one inch, but upon examination a lump was found, practically involving the entire cheek. Some twelve exposures were given, with the gradual reduction of the lump, a moderate dermatitis, and a scabbing. Healing ensued with an excellent appearance. Three months afterward (June 7th) there was a recurrence, the tumor rising to the size of half an egg within two weeks. The *x*-rays were meanwhile constantly applied; but, in spite of a considerable dermatitis, the growth did not subside; ulceration ensued. It then remained quiescent for about a month, when excision was performed (September 15th). The ray is still being applied in the hope of aborting another recurrence. There is no involvement of the surrounding glands, and I see no reason for despair. The lupus patches have entirely healed. The patient's general condition continues excellent.

We have thus reviewed the action of the *x*-ray and, so to speak, have speculated upon its philosophy. Much that has been said is original with the author and purely speculative. He believes, however, that he has an excellent working hypothesis, and that later investigations will confirm his theories. He trusts that they may offer some inducement for research. Be that as it may, he can not close this paper without once more repeating his emphatic denial

that the use of the *x*-ray is entirely empirical. To his mind there is no drug or therapeutical agent whose employment is more thoroughly rational. He asks the question broadly: Is the *x*-ray an empirical agent? He cannot answer in the affirmative.

References.

1. Roentgen Rays in Therapeutics and Diagnostics, p. 263.
2. Journal of Medical Research, 1905, vol. xiii., No. 2.
3. Journal of the American Medical Association, May 13, 1905.
4. Medical News, May 13, 1905.
5. The American Journal of the Medical Sciences, August, 1905.
6. Journal of the American Medical Association, April 1, 1905.

REVIEWS.

ANATOMY: DESCRIPTIVE AND SURGICAL. By HENRY GRAY, F.R.S. Edited by T. PICKERING PICK, F.R.C.S., and ROBERT HOWDEN, M.A., M.B., C.M. New American, from the fifteenth English edition; thoroughly revised and re-edited with additions by JOHN CHALMERS DA COSTA, M.D., Professor of the Principles of Surgery and of Clinical Surgery in Jefferson Medical College, Philadelphia; Surgeon to the Philadelphia Hospital, and Consulting Surgeon to St. Joseph's Hospital. Philadelphia and New York: Lea Brothers & Co.

THE host of friends of *Gray's Anatomy* will cordially welcome this new American edition, thoroughly revised and brought up to date. In the selection of Dr. John Chalmers Da Costa as Editor the publishers have secured a man who is not only widely known as an anatomist and a surgeon but also as a teacher. No better combination of qualifications could be desired to ensure the proper treatment of this most important work. Dealing, as it does, with one of the few branches of medicine which may strictly be regarded as an exact science, no book is better planned to give as much knowledge of human anatomy in a given time. No book is more valuable at the dissecting table as "guide, philosopher, and friend," and no book could give a clearer *résumé* of each subject. The great popularity of *Gray's Anatomy* in the past fifty years, especially among medical students, is sufficient proof of its real and lasting worth. It has stood the test of time better than any of its numerous rivals which have, during that period, appeared in the field against it. This new American edition must not be confused with the Sixteenth edition, published in England in August, 1905, as it is in every way superior to the English version.

To the magnificent array of exquisitely clear-cut illustrations, which have made this book so valuable as an instructor in the past, about five hundred new ones have been added. American, English, French, and German text-books and monographs have been consulted freely, due acknowledgment for original drawings being given to Spalteholz, Cunningham, Poirier and Charpy, Testut, Gerrish, Byron Robinson and the *Atlas of Human Anatomy*, by Carl Toldt, etc. Colors have been freely used to render these illustrations all the more forceful. As to the criticism that may be made of these illustrations being too diagrammatic—which is more especially true of those used

in former editions—it may be remarked that they are all the more valuable to the student on that account. As in the study of geometry, an advance is made from the most elementary propositions to those more elaborate and difficult, so it is best, in the study of anatomy, to fix firmly in the mind a clear understanding of the framework and essential points of the various parts before attempting to master the intricacies of their topographical relations. In this very diagrammatic clearness, therefore, lies one of the greatest charms of the book, as well as one of its greatest virtues. The name of each muscle or part being engraved directly upon it, wherever possible, "is a feature original with Gray and peculiar to his work." Photographs of the actual dissections, no matter how carefully prepared and reproduced, are not nearly so helpful for teaching.

The special articles on Histology and Embryology, found in former editions, have been omitted from this latest American edition, the Editor remarking very properly—" No single volume, in these days, can offer adequate instruction on anatomy, histology, and embryology, and to attempt it would be unwise."

The important bearing that recent developments in embryology have upon the intelligent study of anatomy has, however, been studiously recognized by the Editor. *Résumés* of the essential points of both embryology and histology are given wherever they can throw additional light on the text. Whole sections have been rewritten, especially those parts devoted to the brain, the spinal cord, the nervous system, the abdomen, and the lymphatics. The delightfully instructive paragraphs of Mr. Pick on surgical anatomy "have been modified or added to, in accordance with the views of the day." These surgical notes, embodying as they do the actual experience of countless practical men, aid tremendously in fixing the important facts upon the mind—often bringing order out of chaos by showing clearly to what good use the scientific details may be put.

Taking the volume more in detail one is at once impressed by the large amount of new material and the consequent changes in the text. On the structure of bone, Fig. 1 shows at a glance the several layers of the periosteum, the arrangement of the lamellæ, the component parts of an Haversian system, their relative positions and the position of the endosteum. Who could fail to understand "the fibres of Sharpey" after such a demonstration? The introduction of the new nomenclature in parentheses after the older and more generally used names of the bones, etc., throughout the entire book will undoubtedly tend to lighten the work of the student, "and will facilitate the much-to-be-desired adoption of the new nomenclature." In the description of the temporal bone alone over nine pages is used, whereas in the Thirteenth English edition there are a little over six pages devoted to this subject. In the former there are seven illustrations, in the latter only five. Of these the old

picture of the outer surface of the left temporal has been replaced in the new edition by a more modern and forceful one from Spalteholz. Comparing the new with the older editions no mention is made in the latter of the suprameatal triangle of Prof. Macewen, so important to the aural surgeon, nor of the suprameatal spine or spine of Henle (spina suprameatum). Again, seven pages are given to the superior maxillary bone in the new as compared with five and a half in the old, the result is that in this new edition there is a very much more exhaustive account of the premaxillary bone and its development leading to a clear understanding of the various forms of harelip. Thus instances of the superiority of the new edition might be multiplied considerably did space permit. On the skull, as a whole, there are more than six pages of finely printed matter under "surface form and surgical anatomy." There will be found the fifteen points for fixed measurements and the four equal divisions of the mastoid process (after A. E. Schmitt). Nothing can better serve to first enliven and then crystallize anatomical knowledge than these brilliant surgical notes. Under the "surface form" of the costal cartilages the angle of Ludovic is explained and under surgical notes, among other interesting data, the operations of Estlander, Schede, Fowler, and de Lorme for the resection of ribs are briefly described. On the carpus and tarsus much new material and many new illustrations have been added. So we might multiply instances of change and improvement.

On the Blood Vascular System the text has been most thoroughly revised. The reproductions of the pericardium, as seen from the front and from behind, are exquisitely done; the relation of the thymus gland and ductus arteriosus to the arch of the aorta being well shown. The ligaments of the pericardium are given careful attention, as well as the duct of Cuvier and the oblique vein of Marshall. Illustrations from Cunningham, Spalteholz, Poirier and Charpy and others appear frequently in this section. A particularly striking illustration is that showing the occipital artery and its relations, from a dissection by Mr. Gerald S. Hughes.

The sections dealing with the development of the brain, its blood supply, and its convolutions have been handled with admirable skill. The free use of colors in marking the various subdivisions of the latter render this book the equal of any and the superior of most works on the subject, while one cannot fail to note the clear demonstration of the four divisions of the duodenum and its relations to the pancreas nor how exhaustively the reflections of the peritoneum are traced. The dissection of the vena cava, by Dr. John H. Brinton, illustrates forcibly the valvular arrangement of its tributary veins. Similarly the lymphatics receive the attention their importance deserves and the thoracic ducts are duly impressed upon the mind. We are glad to find the chronological table of the development of the fetus at the end of the book. Objection might be made to

the repetition of the surgical importance of "the suprameatal triangle" on page 86, following similar instruction on page 85, did not such reiteration serve as the keynote of the teacher's success. The general cutaneous distributions of the nerves, conspicuous by their absence in former editions, are strikingly shown in colors. One reads with pleasure the articles on the organs of special sense, welcoming the exquisite reproductions of the work of Cryer on the teeth and Spalteholz on the ear-drum, etc.,

In brief, the further one proceeds in a critical examination of this new American edition of *Gray's Anatomy* the more one is impressed with its numerous excellencies. To praise one part of the book particularly would be to neglect other parts equally deserving of attention. The best of what is known of human anatomy at the present day has been carefully culled and faithfully reproduced. The result is a masterpiece and leaves nothing to be desired. J. P. T.

NOTHNAGEL'S PRACTICE. DISEASES OF THE KIDNEYS AND OF THE SPLEEN, HEMORRHAGIC DISEASES. By DR. H. SENATOR, Professor of Internal Medicine, University of Berlin; and DR. M. LITTEN, Professor of Medicine, University of Berlin; edited with additions by JAMES B. HERRICK, M.D., Professor of Medicine, Rush Medical College, University of Chicago. Authorized translation from the German under the editorial supervision of ALFRED STENGEL, M.D., Professor of Clinical Medicine in the University of Pennsylvania. Philadelphia and London: W. B. Saunders & Co., 1905.

IN the revision of Senator's excellent and exhaustive monograph on the "Diseases of the Kidney," the American editor has had an easy task, but few additions or interpolations having been required. New material has, however, been incorporated under the following topics: General consideration and practical value of cryoscopy, phloridzin glycosuria; the surgical treatment of nephritis and certain practical points bearing upon diagnosis, urinary analysis, and treatment; also some illustrations, all of which distinctly enhance the value of the work. We are somewhat surprised at the fact that the phloridzin test is recommended without any qualifying statements regarding the possibility of deleterious results to the individual submitting to the injections.

The same volume also deals with the "Diseases of the Spleen" and "Hemorrhagic Diseases." The original work of Litten has been further elaborated by Herrick. Among these additions the following are the more important: "Congenital Icterus with Spleno-

megaly," "Splenic Anæmia," "The *x*-ray Treatment of Leukæmia," "The Role of the Mosquito in Malaria," and in the last section of the volume, "Infantile Scurvy." It is to be remembered that the second half of the work deals with these various topics only from the standpoint of the spleen, the major part of many of them being relegated to another volume of the Nothnagel series dealing with the diseases of the blood.

The reputation of the Nothnagel series, as well as the American edition of it, stands on such a high and well-established footing that any further laudation would seem unnecessary. The advantage of a complete and exhaustive reference work of this kind over the numberless smaller text-books which flood the market is too obvious to require comment. G. W. N.

ACUTE CONTAGIOUS DISEASES. By WILLIAM M. WELCH, M.D., Diagnostician to the Bureau of Health and Consulting Physician to the Philadelphia Municipal Hospital for Contagious and Infectious Diseases; for thirty-three years Physician-in-Charge of the Municipal Hospital; Fellow of the College of Physicians of Philadelphia; and JAY F. SCHAMBERG, A.B., M.D., Professor of Dermatology and of Infectious Eruptive Diseases, Philadelphia Polyclinic and College for Graduates in Medicine; Assistant Diagnostician to the Bureau of Health, and Consulting Physician to the Municipal Hospital for Contagious and Infectious Diseases; Fellow of the College of Physicians of Philadelphia; Member of the American Dermatological Association. Illustrated with 109 engravings and 61 full-page plates. Philadelphia and New York: Lea Brothers & Co., 1905.

IN the above work the authors have confined themselves to the discussion of a limited group of maladies which they term the acute contagious diseases, as a subdivision of the infectious diseases would have covered too large a field for their purpose. In the study of these diseases they have had almost unbounded material in the wards of the Municipal Hospital for Contagious and Infectious Diseases of Philadelphia. It is said that this city has had in the last decade or so more epidemics of smallpox and of longer duration and greater severity than probably any other community in America, and it is from a most careful and painstaking personal study of more than 9000 cases of this disease that the material for over half of the work has been gathered and which enables the authors to speak with an authority on the subject that rarely falls to the lot of present-day physicians. Over one-half of the volume is devoted to smallpox and vaccinia: their history, etiology, diagnosis, and treatment. Much space has been given to

the subject of vaccination, the technique, symptoms and course, susceptibility, scars, complications, and statistical evidence of the efficiency of which are of the utmost interest to every student and practitioner of medicine, for everyone must often face the, at times, difficult task of persuading the disbeliever, while comparatively few will ever, in these days, have actual experience with real variola. The illustrations of various phases of these two diseases are excellent and most instructive.

Following these chapters is an article on chickenpox, interesting, not because the disease is *per se* a menace to the health of a community, but because of the frequency with which light attacks of variola or varioloid, have been passed by as simply varicella, thus opening the way for serious outbreaks of the former, and, *per contra*, severe cases of chickenpox sent to the pest houses as smallpox, where, in some instances, they have contracted the more malignant disease with direful results. The diagnosis between the two conditions, especially in times of epidemic, is not always the easy task that the tyro and even many older in the profession might believe.

From a study of over 9000 cases of scarlet fever a most valuable and complete article has been written that appeals to every general practitioner, for he must see and have the care of many such cases in his professional career, and this applies also to the articles on Measles and Rubella. The treatment of these somewhat similar conditions is all that could be desired and appears to be absolutely exhaustive. Nowhere in general works on medicine will so much complete and satisfactory information be obtained, supplemented by such excellent illustrations.

Some 30 pages are devoted to typhus fever, with which the authors have had personal experience; but typhus fever is to-day so nearly an extinct disease, at least in the western hemisphere, that a more lengthy dissertation is not deemed necessary.

Finally, diphtheria, receives all the consideration that should be given to a contagious disease that seems to be endemic in all large communities and to which all small ones are subject to periodical outbreaks. The diagnosis, from a clinical and bacteriological standpoint, is gone into in detail; the prophylactic and curative value of the antitoxin treatment, with its possible complications, is discussed, and the procedure of intubation is fully explained, with the aid of the best and most illustrative cuts that have yet appeared to aid the novice. The authors have found in their experience in the Municipal Hospital of Philadelphia, as have other observers, that as good results are obtained with moderate doses of antitoxin in the treatment of diphtheria as with very large ones, but that, on the other hand, no harm has resulted from the use of even very large quantities of serum. They lay stress on the necessity of early treatment to secure the best results, as do other writers, and are agreed with

them as to the very great protective power it exercises in those exposed to contagion.

A short chapter at the end of the book on Disinfection is of value. The volume is well arranged and written in an attractive and readable style, with a profusion of illustrations, well portraying the conditions described. While the subject is limited to the six or seven diseases characterized as "acute contagious," they are so exhaustively treated as to swell the work to 781 pages, but the reader's interest is carried through to the end. The record of the personal observations of the authors runs through the whole book and makes it an addition of unsurpassed value to the literature of the subject.

G. M. C.

A Dictionary of New Medical Terms. Including upward of 38,000 Words and Many Useful Tables, being a Supplement to *An Illustrated Dictionary of Medicine, Biology and Allied Sciences.* By George M. Gould, A.M., M.D., author of *The Student's Medical Dictionary, 30,000 Medical Words Pronounced and Defined, The Meaning and Method of Life, Borderland Studies;* editor of *American Medicine,* etc. Based upon recent scientific literature. Philadelphia: P. Blakiston's Son & Co., 1905.

As the author states in his preface to the above volume, "nothing so well illustrates the astonishing vitality and progress of present-day medical science as its unparelleled multiplication of new words." And in good truth it is amazing that well over 30,000 new words and terms should have been added to the medical vocabulary during the ten years that have intervened since Gould's *Medical Dictionary* was first given to the public. And yet in a science that is continually making such rapid progress as medical science is, it is easy to see that new discoveries and steps in advance must be tagged and indexed with new terms; and this is a dictionary primarily of new terms, though many obsolete forms are included for the benefit of the historian and student of old medical works. It is in every way a supplement to the *Illustrated Dictionary of Medicine, Biology, and the Allied Sciences,* containing not only the new words coined since the first edition, but also all errata and addenda of the successive editions that that most successful work has passed through, and it brings the latter thoroughly up to date in all respects.

Many tables of value and interest have been added, such as those giving the various stains, tests, and reactions used by the pathologist; signs and symptoms, treatments, and many others too numerous to mention. The book shows a vast amount of painstaking care and labor, as can readily be imagined. It is a work of merit and very much to be commended. G. M. C.

TEXT-BOOK OF HUMAN PHYSIOLOGY: INCLUDING HISTOLOGY AND MICROSCOPICAL ANATOMY, WITH SPECIAL REFERENCE TO THE PRACTICE OF MEDICINE. By DR. L. LANDOIS, Professor of Physiology and Director of the Physiological Institute in the University of Greifswald. Tenth and enlarged edition, edited by ALBERT P. BRUBAKER, M.D., translated by AUGUSTUS A. ESHNER, M.D. With 394 illustrations. Philadelphia: P. Blakiston's Son & Co., 1904.

THIS, the fifth edition in English of Professor Landois' interesting physiology, a translation of the tenth and latest German edition, speaks for its popularity. Since the last English edition Professor Stirling's, in 1891, the treatise has been revised three times by the author, and owing to the important contributions made to the science of physiology in the last ten years, the present translation should be heartily welcomed. The author considers that clinical medicine rests upon a basis of physiology and pathology and in his treatise continually reminds the reader that disease is dependent upon the perverted functions of one or several organs. The muscle-nerve preparation and several other subjects which figure so prominently in the usual text-book of physiology are subordinated to discussions upon the physiology of the blood, cordeodynamics, problems of metabolism, and the mechanism of digestion. Portions of all the sections are devoted to microscopical anatomy and pathology; and indeed, in many places the symptomatology of disease figures quite prominently. In fact, the book deals with clinical rather than experimental physiology. The omission of references to such important investigations as Pavlow's work upon digestion, certain recent contributions concerning the coagulation of the blood, and the latest researches upon the physiology of the pancreas is noteworthy. The scope of the book is, however, very extensive and in every instance the descriptions and explanations are of necessity concise. The book is excellently paragraphed and the translation is satisfactory. It contains 1006 pages.

W. T. L.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Case of Malignant Pulmonary Endarteritis after Gonorrhœa, Simulating Disease of the Pulmonary Valve.—FURTH and WEBER (Edinburgh *Medical Journal*, July, 1905, p. 33) report a case in which the ante-mortem diagnosis was thought to be malignant endocarditis of the pulmonary valves, with incompetence of the pulmonary valve. The patient, a man, aged twenty-seven years, had had two attacks of gonorrhœa, one two years and the other five months before the patient came under observation. For two weeks he had suffered from daily chills, with fever and headache. When he was first seen the apex impulse of the heart was in the normal position. The chief feature in connection with the heart was the presence of a rough systolic and diastolic double murmur in the second left intercostal space. The first and second sounds were here audible. There were urethral threads in the urine, but no gonococci were found. The patient remained under observation until his death seven months afterward. The intermittent fever, with the exception of a short interval of a few days, continued up to the time of death. Both murmurs at the pulmonic area persisted and the long, rolling, or mill-like diastolic murmur had its maximum intensity in the second left intercostal space about an inch to the left of the sternum. There is no note of blood cultures having been made during life. The heart became moderately enlarged, particularly toward the right.

At autopsy it was found that all of the cardiac valves were normal. On the anterior wall of the pulmonary artery, however, about three-quarters of an inch above the pulmonary valves, was a rough, warty outgrowth, oval in shape, about one inch across in its longest diameter, and projecting about one-eighth of an inch from the inner

surface of the artery. Stained specimens showed masses of cocci, some arranged in definite streptococcal chains. The statement is made that no typical gonococci could be detected. Blood cultures were apparently not made. The bacteriological report is not as full as one would wish for.

The writers discuss two special points in connection with the case. In the first place, they think that the diastolic murmur at the pulmonic area, considering that the valves were normal, may have been due to relative incompetence of the pulmonary valves, owing to the dilatation of the pulmonary ring. Further, they made a distinction between a gonorrhœal and a gonococcal endocarditis. In the latter the endocarditis is due to the gonococcus itself; in the former, the causative agent may be a streptococcus or staphylococcus, which has gained admission to the circulation in the urethra through a portal of entry caused by the gonorrhœal urethritis. Lenhartz, Keller, and Heller have reported such cases.

It is claimed that this is the first instance of an acute malignant endarteritis of the pulmonary artery that has ever been reported. There are records of such lesions in the aorta, however.

The Etiology of Syphilis.—Flexner (*Medical News*, December 9, 1905, p. 1105), in the Carpenter lecture recently delivered in New York, reviews the literature up to date concerning the spirochæta pallida and its etiological relationship to syphilis. He also gives an account of his own personal investigations on the subject.

It is pointed out that all organisms discovered previous to the spirochæta pallida and thought to be the specific organisms of syphilis have been conclusively shown not to have any etiological bearing on the disease. The spirochæta pallida was discovered and named by Schaudinn and Hoffman. They found it in the primary sore, the adjacent enlarged glands, and in the flat condylomata of syphilitic patients. Their first published report appeared in April, 1905. The organism measures 4 to 10μ, the average length being 7μ, or about that of a red blood corpuscle of man. In width it varies from unmeasurable thinness to 0.5μ. It possesses from three to twelve, sometimes more, curves, which are sharp and regular and resemble the curves of a corkscrew. The poles are sharpened. The organism is mobile and the motions consist of rotations on the long axis, forward and backward movements, and bending of the entire body. Flagella have not been seen. Another spiral organism is found normally in the skin of the genitalia and on the surface of non-syphilitic ulcers. Schaudinn and Hoffman proposed tentatively for it the name spirochæta refringens. Flexner conveys the impression that it can be recognized morphologically from the pallida. The spirochæta is very refractory to stains, and being usually scanty in the lesions, is very difficult to find. It stains best with azure blue.

The spirochæta pallida has been found in the following superficial lesions of the secondary stage: condylomata; macular, papular, and pustular skin lesions. Of the deeper structures in this stage in which the organism has been found are the lymphatic glands and spleen. In rare instances it has been found in the circulating blood.

The organism up to the present has not been with certainty found in the lesions of the tertiary stage of the disease.

A number of observers have also found spirochæta pallida in the pemphigus bullæ and papules of the skin in congenital syphilis.

In 1903 Metschnikoff and Roux announced to the world for the first time, and gave ample proof of their statements, that the higher or anthropoid apes were subject to syphilitic inoculation, the disease manifesting itself in the form of primary lesions, which, after an interval of time, are followed by adenitis and an eruption of syphilitic papules. Metschnikoff, Flexner, and Kraus have found the spirochæta pallida in the experimental primary syphilides of monkeys. Kraus, in fact, traced it through two monkeys, the second animal having been successfully inoculated with the virus of the first.

Although giving the impression that the spirochæta pallida plays a very important part in the etiology of syphilis, Flexner says: "I am still far from having myself a conviction of its position as immediate cause of that disease, for the establishment of which causal relation more stringent proof than yet produced will be required."

SURGERY.

UNDER THE CHARGE OF

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Congenital Luxation of the Hip; Pathological Anatomy; Premonitory Lesions.—DAMANY (*Revue de chirurgie*, July, 1905) states that, while the well-developed lesions of congenital luxation of the hip have been revealed long ago, the anatomical deformations preparing the way for it have been unrecognized. They are not the effect of the luxation, because they precede it in date, and, being slight, are capable of spontaneous and complete correction. They are not the cause, properly speaking, since they are necessary to its realization. They are the first manifestations of the pathological tendency. They consist of the deformation of the cotyloid cavity and of the femoral head. They are found in non-luxated hips and there indicate a simple predisposition to the luxation or characterize its preparatory phase. When they are sufficiently intense they inevitably result in luxation.

Congenital luxation does not exist at birth, but is accomplished during the first year of life. The too great obliquity forward of the cotyloid cavity, and the too great torsion of the femur give to the articular surfaces an impaired reciprocal relation to each other. In the dorsal decubitus and in the upright position the axis of the superior ephysis is of the femur is parallel to the plane of the cotyloid cavity. The forced extension necessary for this position is without unpleasant consequences, when the pathological tendency is moderate; but if it is excessive, the head of the femur is turned out of the depth of the coty-

loid cavity, so that this gradually becomes filled and the luxation unexpectedly occurs.

The leveling of the cavity ought only to be exceptionally sufficient at the time of birth to permit an immediate luxation, so that luxations at birth are exceedingly rare if they exist at all. But the filling of the cavity some months after birth may have progressed so far that the action of the longitudinal muscles, aided or not by the weight of the body, brings about the ascension of the head and its escape from the cotyloid cavity. The cavity, if of little depth in the newborn, becomes still less in the first months after birth and predisposes to luxation, because of the lack of support to the head. The extensor muscles tend to draw the head out of the cavity, the longitudinal muscles aid in this and to make it ascend.

The pressure on the head is from without inward and from above downward by the superior part of the cotyloid cavity and particularly by its cotyloid cartilage. The cartilage is thus flattened above, where it is pressing hardest against the femoral head. The cotyloid cavity thus becomes oval in contour and elongated. The anterior and posterior margins become more prominent, but anteroinferiorly and posterosuperiorly the cavity is very shallow and flattened. Thus the escape of the head is rendered easy.

Abnormal diminution of the depth of the cavity, oval elongation of it, disappearance of the prominent margins above, and of the cotyloid cartilage in the posterosuperior region, are the lesions of the cotyloid cavity premonitory to the luxation.

The deformations of the femoral head are the result of the changes in the cotyloid cavity. A reciprocal flattening occurs and the head is elongated from above downward. The round ligament is elongated and forms for itself a groove in the posteroinferior part of the head.

With regard to the etiology of these malformations, it may be said that they always coexist with an exaggeration of the forward obliquity of the cotyloid cavity or the torsion of the femur, or both defects are combined. The total default is always greater than the average normal. It is equal to or greater than the maximum theoretically compatible with good function of the joint.

Contribution to the Study of Functional Impotence Consecutive to Articular Traumatism.—MALLY and RICHON (*Revue de chirurgie*, May, 1905) terminate an extensive article on this subject with the following conclusions:

1. In every functional impotence consecutive to articular traumatism, one should always think of a spinal involvement, closely allied to the joint condition, of which the reflex muscular atrophy is the most evident and best-known manifestation.

2. To the well-known symptoms of reflex atrophy (atrophy itself, paresis, spasmodic phenomena, diminution of galvanic and faradic excitability without the reactions of degeneration), it is necessary to add diminution of electric resistance compared to the sound side.

3. The reflex atrophy may be fatal when there is developed a joint effusion. All degrees may be present, from the simple paresis to the absolute paralysis, which is very rare.

4. Pathological anatomy and experimentation have shown that the chief medullary lesion consists in a diminution of the large motor cells of the anterior horn. In the nerves and muscles there are disseminated

among the healthy elements some degenerated articular sensory fibres, some degenerated motor fibres, atrophied muscular fibres, thus constituting lesions of the reflex arc and giving definite assent to the theory of Vulpian and Charcot.

If centripetal excitability of articular origin is capable of changing so profoundly the motor cells in the anterior horn, it is equally capable of altering the trophic centres, which preside over the nutrition of all the other periarticular tissues, and which, in fact, are often altered.

Aside from the lesions of the large motor cells, there are probably other medullary changes still unknown, which the progress of pathological histology will some day make evident.

The medullary lesions exist in two different degrees or conditions: (*a*) A dynamic condition, susceptible of cure and without lesions perceptible by the ordinary methods of investigation; (*b*) a condition characterized by the presence of material lesions of nerve centres, particularly the motor centres, bordering on degenerative atrophy of the muscular fibres and on incurability.

5. The conception of reflex muscular atrophy ought to occupy an important place in general surgical pathology. It clears up the pathogenesis of a great number of articular affections; passive displacement of the humerus, painful flat foot with valgus, acquired painful deformed hip, genu valgum of adolescents, scoliosis of adolescents, etc.

6. There is no necessary relation between the intensity of the articular affection and the gravity of the reflex muscular atrophy which it provokes. But there is a relation between the duration of the joint affection and the gravity of the reflex muscular atrophy which it causes; the more prolonged the articular irritation, the less chance of curing the medullary lesions. The atrophy is habitually worse in the lower extremity; the mechanical excitations of walking, always premature during convalescence, offering the only explanation.

The reflex atrophy will be as much more rapidly cured, as the causal-joint lesion will itself have been cured. If the joint trouble recurs, the muscular atrophy will reappear. If the joint trouble becomes chronic, the muscular atrophy will become incurable. Even in a functional cure the reflex atrophy following every joint affection leaves after it, almost always, some persistent vestige, easily revealed by electric exploration.

7. Electric exploration usually permits one to establish the prognosis of a reflex muscular atrophy; it is as much more grave as the galvanic excitability is diminished, compared to the sound side.

8. The benign form of reflex muscular atrophy justifies faradization, or better, the static spark (franklinization), of which the technique is much more simple. When the spasmodic phenomena take on a notable importance localized faradization is dangerous. It is necessary to substitute for it static electricity, under the sedative form (static bath, static electricity localized to the affected parts, brush, revulsion with the sparks on the vertebral column).

In the incurable forms static electrotherapy is still more helpful to attenuate or cause to disappear the spasmodic and painful phenomena of the more troublesome cases. The spasmodic phenomena contra-indicate absolutely besides faradization, all the violent manœuvres directed against the joint or the atrophied muscles (forced mobilization, premature functional movements, massage, etc.).

Those are the spasmodic phenomena (exaggeration of the tendinous reflexes, exaggeration of the mechanical excitability of the muscles,

rapid fatigue with contractures) which are the necessary practical guide to the prudent and reasonable direction of the treatment, the test of its innocuity, and of its efficiency.

Final Results in the X-ray Treatment of Cancer, Including Sarcoma.—COLEY (*Annals of Surgery*, August, 1905) draws the following conclusions on this subject considered up to the present time.

1. That the *x*-ray exerts a powerful influence upon cancer cells of all varieties, but most marked in cases of cutaneous cancer.

2. In some cases, chiefly in superficial epithelioma, the entire tumor may disappear, probably by reason of fatty degeneration of the tumor cells with subsequent absorption.

3. In a small number of cases of deep-seated tumors, chiefly cancer of the breast and glandular sarcoma, tumors have disappeared under long treatment by the *x*-ray. In nearly every one of these cases, however, that has been carefully traced to final result, there has been a local or general return of the disease within a few months to two years.

4. In view of this practically constant tendency to early recurrence, furthermore, in the absence of any reported cases well beyond three years, the method should never be used except in inoperable cases, or as a prophylactic after operation, as a possible, though not yet proven, means of avoiding recurrence.

5. The use of the *x*-ray as a preoperative measure in other than cutaneous cancer is contraindicated: (1) Because the agent has not yet been proven to be curative; (2) because of serious risks of an extension of the disease to inaccessible glands or to other regions by metastases during the period required for a trial of the *x*-ray.

Fractures of the Spine.—BURRELL (*Annals of Surgery*, October, 1905) divides fractures of the spine into two classes—those with injury to the cord and those without.

The treatment of an individual case cannot be decided from the statistics, because the lesion varies so widely. Only an open operation in many cases will decide whether the cord is crushed or pressed upon by bone, blood, or an exudate. Total transverse destruction of the cord can be diagnosticated only by the persistent total loss of reflexes, complete insensibility to touch and pain, and motor paralysis below the level of the lesion. If pressure on the cord is allowed to remain for many hours irreparable damage to the cord may take place.

Unless it is perfectly clear that the cord is irremediably damaged, an open operation to establish the condition of the cord and to relieve pressure is imperative as soon as surgical shock has been recovered from. In certain fractures of the spine, when the cord is not injured, but is liable to injury from displacement of the fragments of a vertebra, rectification of the deformity and fixation of the spine may be used. If the cord is crushed, no matter what the treatment, there will of necessity be a high rate of mortality.

Tuberculous Conditions of the Spine Requiring Surgical and Mechanical Relief.—WILLARD (*Annals of Surgery*, October, 1905) states that the prime factors in securing new bone formation to replace carious bone are complete methodical and long-continued fixation of the spine in the position of hyperextension, with healthy surroundings in the sunlight.

Laminectomy for paraplegia is advisable only after a prolonged treatment of one to two years along the above lines, and then only in selected cases, where the loss of motion and sensation are progressively worse and the symptoms threaten life. Cases of non-improvement and death equal nearly 65 per cent.

Forcible and immediate straightening of the kyphosis is an unsurgical and dangerous proceeding. Forcible gradual straightening by supporting the kyphotic area upon a pedestal is a valuable agent in relieving deformity. Complete erasion of the carious bodies of the vertebræ is an uncertain operation. Wiring of the spinous processes has never been sufficiently tried to demonstrate its helpfulness. Spinal abscesses which contain only liquefaction of caseation should be aspirated. When true pus has formed aseptic drainage is advisable.

The Surgical Treatment of Intraspinal Tumors.—HARTE (*Annals of Surgery*, October, 1905) found records of 92 operations for spinal tumors, among which 43 patients died, a total mortality of nearly 47 per cent. Of these he estimates that about 28 per cent. were due to the operation itself, and thinks that the relief obtained, even if no cure results, justifies the operation.

It has usually been stated that the extradural tumors were much more frequent and much less fatal than intradural growths. Harte did not find the frequency of the extradural much higher, while their mortality was much greater.

In performing the operation the opening in the dura should be small and the escape of the cerebrospinal fluid, which may prove a veritable flood, should not be permitted to occur too rapidly. No alarm need be felt at the quantity of this fluid evacuated, since, so far as the writer is aware, no evil results have been known to follow the plan usually adopted of letting it flow until it stops of its own accord.

If the dura has been opened it should be sutured, if at all, very loosely. These patients have done much better when the drainage of cerebrospinal fluid after the operation has been free.

Studies in the Surgical Anatomy of the Small Intestine and Its Mesentery.—MONKS (*Annals of Surgery*, October, 1905) says that the nature of his paper does not admit of a satisfactory summary of all the points which have been spoken of in it.

He divides the mesentery roughly into a proximal or flat portion, representing about two-thirds or three-fourths of its length, and a distal or ruffled portion, about one-third or one-fourth. The fold of mesentery descending into the pelvis can usually be palpated from a wound in the lower abdomen, and forms a valuable guide for the finger in the attempt to reach the left abdominal fossa. The free border of the gut is several feet longer than the mesenteric border when the gut is freed from the mesentery.

The kinks in the intestine are usually confined to the lateral aspect of the gut. Unless the intestine be "gathered up" on the tube, it is impossible to pass any instrument, hard or soft, straight or curved, into the gut without the possibility of soon engaging the wall of the intestine, usually in its free border. The surest method, at least on the cadaver, of determining which is the proximal and which is the distal end of a loop of intestine, is by palpation of the mesenteric root between the thumb and fingers of one hand.

A Study of Infection of the Knee-joint Based upon an Analysis of 310 Cases.—FLINT (*Annals of Surgery*, October, 1905) divides the cases into five groups, according to the mode of infection: (*a*) Clean knees operated. (*b*) Penetrating wounds of the knee-joint. (*c*) Primary in the knee without evident port of entrance. (*d*) In the course of evident infections elsewhere. (*e*) Following some trauma (non-perforating).

In the absence of bacteriological examination some cases of infection cannot be distinguished from some of those due to trauma and those possibly due to toxins secondary to infection elsewhere. Flint believes that the knee-joint has certain germicidal powers. Most knee-joints which have been infected, opened and drained, and recovered, show varying degrees of functional disability from slight limitation of motion to complete ankylosis, with or without subluxation.

The average stay in the hospital of an infected knee-joint was between two and three months. When it is once decided to open and drain a knee-joint the operation should be as radical as possible from the start. The position of the leg should be that giving the best drainage—*i. e.*, the patient should be face down.

Penetrating wounds of the knee give the greatest risk of infection; operations upon clean knees and where there has been no recent trauma give the least risk of infection.

THERAPEUTICS.

UNDER THE CHARGE OF

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Carbonic-acid Baths in Cardiac Conditions.—DR. HIRTZ prefers the natural to the artificial bath, since the gas in the former is evolved more slowly and regularly, and considers that this means of treatment is an excellent one in various forms of heart weakness. Relief is experienced as soon as the tiny bubbles begin to collect upon the skin; a pleasant warmth diffuses itself through the body, respiration becomes more full, the pulse becomes slower, and the blood pressure lower. If irregularity is present it is diminished. If there is abnormally low blood pressure, this becomes higher; after the bath it falls again, but in hypertension the decrease in pressure is more permanent. The baths are indicated in vascular lesions as soon as disturbance of compensation appears. If venous stasis is present this condition, with its attendant symptoms, albuminuria, etc., will be relieved. In mitral stenosis the treatment is not very effectual, and in aortic lesions it is seldom indicated. In beginning arteriosclerosis the baths are useful unless the coronary arteries are involved; in this case they are absolutely contraindicated. If excessive tension with weakness of the heart muscle is present this symptom may be relieved by the baths. Sclerotic patients with hypo-

tension may be relieved of dyspnœa, their tendency to tire easily and to bronchitis. The treatment is effectual also in cardiac asthenia occurring in emphysematous patients, in the obese, in convalescent conditions, etc.—*La presse médicale*, 1905, No. 42, p. 331.

Barium Chloride in Cardiac Conditions.—Dr. E. Miesowicz has used barium chloride in cases of cardiac insufficiency which were not benefitted by simple rest in bed and diet regulation. The dose employed was $\frac{4.5}{100}$ of a grain or less, repeated two or three times daily, two hours after eating; two hours later the pulse and the blood pressure were measured, the state of the urine was examined and the weight and general condition noted. The author concludes that barium chloride acts especially upon the blood pressure, which it rapidly lowers, that it is useful in the minor types of cardiac insufficiency, but on the whole, he considers the drug inferior to digitalis.—*La semaine médicale*, 1905, No. 24, p. 283.

The Treatment of Erysipelas.—Dr. I. S. Maximoff recommends the following local and constitutional treatment: The former consists of dressing the seat of the disease two to four times daily with guaiacol, iodine tincture, and alcoholized ether of each 75 minims, essence of peppermint, q. s. Internally he gives camphor, which has also been advocated by the celebrated Pirogoff. The drug may be administered in powdered form, 1.8 grains every two hours up to 12 to 22 grains during the day, or preferably in solution, as per the following formula: Powdered camphor, 1.5 parts; bitter almond or cherry laurel water, 2 parts; almond milk, 120 parts; simple syrup, 30 parts; a dessertspoonful every hour and a half, and follow the dose by a hot drink—weak tea, chamomile tea, or the like. The administration of the camphor is continued until moderate diaphoresis is established, this symptom marking the crisis, after which the disease usually subsides.—*Revue française de médecine et de chirurgie*, 1905, No. 24, p. 569.

Scopolamine-Morphine as an Adjunct to General Anæsthesia.—Dr. M. G. Seelig reports a series of 65 cases in which scopolamine hydrobromate, gr. $\frac{1}{100}$, and morphine, gr. $\frac{1}{6}$, were administered a half an hour before general ethyl-chloride-ether anæsthesia was induced. From the results he concludes that there is no objection to the use of these drugs in these doses and that their administration is a boon to both patient and operator. Of the 65 cases, only 1 vomited or retched while on the table; 77 per cent. of them did not vomit at all, and one-third of those that did vomit did so but once and then only a little mucus. Nausea was marked in but 2 cases, and the vomiting occurred in every case more than two hours after the operation, which is an important consideration, for by that time laryngeal sensibility had returned and there was no danger of aspiration pneumonia. In addition, the quantity of the general anæsthetic necessary was greatly lessened, a little more than 2 ounces per hour being all that was used; the drugs induce a peaceful state of mind on the part of the patient, and the stage of excitement is eliminated, likewise there is no excitation during the recovery of consciousness, and there is also freedom from pain. Still another advantage is the fact that salivation during the operation is absent.—*Annals of Surgery*, 1905, No. 2, p. 185.

OBSTETRICS.

UNDER THE CHARGE OF

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Cholecystectomy in the Seventh Month of Gestation without Interrupting Pregnancy.—In the Bulletin of the Lying-in Hospital, New York, June, 1905, DAVIS reports the case of a patient, seven months pregnant, admitted to the hospital, having had jaundice, and with a temperature of 102.2° F. Liver dulness extended from the sixth rib to the border. Over the gall-bladder was localized tenderness and rigidity. The patient was put to bed, cold applied over the tender region, morphine given to relieve pain, and the intestinal tract cleared by calomel. A hot pack was given. The patient made a rapid recovery. After acute symptoms had subsided operation was performed, great difficulty being found in keeping the intestines aside, as the pregnant uterus pushed them up into the wound. The gall-bladder was small, filled with small stones and gravel. The gall-bladder was excised and the abdomen drained by a strip of iodoform gauze. The patient made a good recovery, and four weeks after the operation was threatened with labor. This subsided until thirteen days later, when the membranes ruptured spontaneously, podalic version was done, and a premature fœtus extracted. The child lived twenty-four hours. The mother made a good recovery.

Spontaneous Rupture of the Clavicle in Birth in Vertex Presentation.—HAUCH (*Zentralblatt für Gynäkologie*, 1905, No. 33) has collected 16 cases of labor in vertex presentation in which the clavicle was broken. The children were all above the average size, with one exception. In 7 the right clavicle was broken; in 9 the left. In 3 cases the forceps was used; in 1 the pelvis was contracted, and in 1 difficulty was experienced in bringing down the shoulders. The fractures were subperiosteal and a good result was obtained. The immediate cause of the fracture was thought to be traction upon the head to deliver the body and failure in the normal mechanism of the delivery of the shoulders.

The Treatment of Eclampsia by Bleeding and Saline Transfusion.—JARDINE (*Journal of Obstetrics and Gynecology of the British Empire*, July, 1905) reports 15 cases of eclampsia treated by bleeding and saline transfusion. One drachm of acetate of sodium was added to a pint of normal salt solution. Patients were freely purged and hot packs were used. From 12 to 20 ounces of blood were taken and 2 pints of the solution injected into the vein.

As regards delivery, forcible delivery is not advised. When, however, the os is nearly or fully dilated the pregnancy should be terminated. Morphine was not used, chloral and bromide being given if necessary. In 1 case ethyl chloride was used to lessen the pain of hypodermoclysis, and this was followed by the sloughing away of the skin which had thus been frozen. One patient's recovery was complicated by phlegmasia, and this patient had a very severe attack of dyspnœa which gradually ceased.

Hæmatoma of the Labium during Labor.—JONES (*British Medical Journal*, October 14, 1905) reports the case of a primipara, aged thirty-five years, in whom the head failed to descend and was brought into the pelvic cavity by forceps. The birth of the child occurred spontaneously.

About two hours before birth painful swelling was observed in the right labium, which increased in size until it was as large as an egg. As it threatened to cause a laceration it was incised, when liquid venous blood escaped. The pressure of the head caused the vaginal wall to rupture over the tumor and force out from the tumor a clot of considerable size. The laceration thus made was closed by suture and the patient made ultimately a good recovery.

GYNECOLOGY.

UNDER THE CHARGE OF

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Treatment of Uterine Cancer.—FLATAU (*Münchener Med. Wochenschrift*, 1905, No. 11) reports 259 cases of cancer of the uterus out of 13,243 gynecological cases treated at the Nuremburg Clinic in twelve years (1.95 per cent.); 121 (46.7 per cent.) were operable by the abdominal route, which has been adopted exclusively during the past three years: 95 hysterectomies were performed, including 75 vaginal (with 3 deaths), and 22 abdominal, with 22 deaths; 12 patients were free from recurrence at the time of writing, 8 being cases of cancer of the body of the uterus.

The symptoms which called attention to the presence of the disease, leucorrhœa and hemorrhage, were noted for periods of from two weeks to one year. In 10 per cent. of the patients who had been under medical treatment 10.4 per cent. had never been examined. The writer hopes that better results will be obtained by earlier operations, but is not sanguine about the ultimate results to be obtained by the radical abdominal method.

Venous Uterine Fibroids.—KNAUER (*Zentralblatt für Gynäkologie*, 1905, No. 42) describes 4 cases which seemed to belong to a distinct class of fibromyomata hitherto undescribed. They were distinguished histologically by the fact that the growths developed partly in the muscular layer of the wall of the veins, and partly within the lumina, forming small projections covered by the endothelium and intima.

The writer infers that either small myomatous nodules in the neighborhood of the vessels may form metastases within the veins, or that the myomata actually develop in their walls, either singly or in multiple form.

Tubal Menstruation.—STEINBUCHEL (*Zentralblatt für Gynäkologie*, 1905, No. 42) describes a case in which a periodical discharge of blood

occurred from the end of a Fallopian tube, included in the cicatrix after a vaginal hysterectomy, the patient having at the same time the usual subjective feelings of normal menstruation. A microscopic examination of the tube (which was subsequently removed on account of persistent pain) showed that it was perfectly normal. The writer infers that a true menstrual flow never occurs from a normal tube, although under the influence of the monthly congestion slight hemorrhages may take place into the tissue of the tube, especially just beneath the epithelial layer. Pathologically, the blood pressure may be so extreme that blood exudes from a diseased tube coincidently with the menstrual flow. A diseased tube remaining after removal of the uterus may be the origin of typical hemorrhages. Exceptionally, when the uterus is absent, normal menstruation may be replaced by hemorrhages from a normal tube.

Relaxation of the Uterine Muscle in Relation to Curettement.—VAN TUSSENBROEK (*Zentralblatt für Gynäkologie*, 1905, No. 42) introduced this subject for discussion before the Dutch Gynecological Society, the members of which differed considerably with regard to the varying tonicity of the muscular wall of the uterus. KONWER, as well as the reader of the paper, stated that he had repeatedly made this observation, in which STRATZ agreed with him. PERSINANE and POMPE had both noted a sudden relaxation of the organ while introducing tents. In reply to questions, the reader stated that he believed that alternate contraction and relaxation of the uterus occurred without reference to narcosis. The sudden giving way of the sphincter at the os internum during the insertion of a tent or finger was, in his opinion, by no means a proof that laceration of the cervix had occurred.

OPHTHALMOLOGY.

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Some Late Statistics upon Blindness.—SALZER (*Münchener med Wochenschrift*, 1905, Bd. xxviii.) has made an analysis of the statistics upon the blind in Bavaria recently compiled by A. Schaider, of the Central Institute for the Blind, in Munich. These statistics show that the number of those who have lost their sight through blennorrhœa has not diminished, proving that the Credé method of prophylaxis is not sufficient. The majority of those blind from blennorrhœa do not arise in institutions or in the better classes in private practice, but from the poorer classes, especially in the case of illegitimate children, and largely also from the incredible ill-will on the part of midwives, who, in spite of legal and other warnings, often dissuade the parents from calling in a

physician. He concludes, as had also H. Cohen before him, that legal compulsion of midwives to report all cases of blennorrhœa and less conservative treatment of an eye which threatens danger to the other from sympathetic inflammation are the most important lessons to be drawn from these latest Bavarian statistics. Increased knowledge on the part of the public regarding matters of hygiene and prophylaxis must do the rest.

The Pathological Histology of Parinaud's Conjunctivitis.—VERHOEFF and DERBY (Zehender's *Klin. Monats. f. Augenh.*, June, 1905) report the histological findings from a case of Parinaud's conjunctivitis.

The changes consisted essentially in pronounced cell necrosis in the subconjunctival tissue, with widespread infiltration of the latter with lymphoid cells and phagocytes. There was, in addition, a chronic inflammatory condition of the deeper structures, which resulted in the organization and production of new connective tissue. Parinaud's conjunctivitis has no relation to lymphoma of the conjunctiva of adults, to which it has but slight or no resemblance clinically or histologically. The diseases which resemble it most are trachoma and tuberculosis of the conjunctiva.

Central Scotoma in Congenital Amblyopia.—HEINE (*Klin. Monatsb. f. Augenh.*, January, 1905) defines congenital amblyopia by the three following characteristics: 1. Permanent diminution of the visual acuity, slight or well marked. 2. Normal ophthalmoscopic appearance. 3. Integrity of the refracting media.

The cause of congenital amblyopia is to be sought in the presence of a central scotoma, which is present in 90 per cent. of the cases. In this connection, the author gives some very interesting measurements of the visual fields.

Lesions recognizable by the ophthalmoscope are rare. They may, however, be present. The macula may be deeper in color. Loss of tissue may also occur in the macular region. The central scotoma is round or oval, absolute or relative, most frequently monocular. The periphery of the field is intact, though occasionally there may be slight concentric contraction. Two hypotheses seem to explain the central scotoma: it may be the result of a functional disturbance, which dates back to earliest infancy; or the trouble is congenital, and due to an anatomical lesion. The latter is the more probable hypothesis.

Rupture of the Choroid.—OHM (Inaug. Dissert., Giessen, 1905, reviewed in *Centralblatt f. Augenh.*, October, 1905) has collected 316 reported cases of this accident and adds 5 of his own. The ruptures have generally occurred indirectly, and in a few cases even without the globe itself experiencing direct violence. Accordingly, they are generally located in the posterior half of the bulb, especially the temporal portion. The typical form is the crescent; with the radial next. There may be as many as five or more separate ruptures. The retina is torn only in a small proportion of the cases, generally at the same spot. The prognosis as to sight is, as a whole, not very favorable; this is in part due to other injuries occurring at the same time as the rupture. Of the writer's own cases, 2 are very rare; in 1 the convexity was directed toward the papilla. In the other the main rupture almost encircled the macula without, however, uniting in a complete circumference.

Late Results of Removal of the Clear Lens in High Myopia.—Marx (Inaug. Dissert., reviewed in *Centralblatt f. Augenh.*, October, 1905) has analyzed 65 cases of the results of this operation. In 10 (15.4 per cent.) detachment of the retina occurred. This percentage is decidedly higher than that of previous statistics; the detachments are certainly to be ascribed in part to the operation, for the same event occurs only in 6.5 per cent. of the cases of high myopia without operation. The writer, nevertheless, would not reject Fukala's operation altogether, in view of the great advantage it gives to the large majority of eyes operated upon. The danger is to be minified by a proper technique; above all, too deep incisions into the lens with wounding of the posterior capsule are especially to be avoided; such may readily lead to prolapse of the vitreous into the anterior chamber. Extraction with the lance knife is to be avoided as far as may be; discission for secondary cataract, although not altogether avoidable, even with most perfect technique, is particularly dangerous and should be practised with all conservatism possible.

Von Hippel (*Deutsche med. Wochenschrift*, 1905, Bd. xxvi.) defends the operation. He believes that postoperative detachments of the retina are due to the myopia rather than to the operation. He holds, however, that the operation requires certain definite indications before it is justifiable.

Amblyopia from the Fumes of Wood Alcohol.—Hawes, Lynn, Mass. (*Boston Medical and Surgical Journal*, November 9, 1905), reports the case of a man, aged fifty-three years, who showed profound intoxication after working three days with wood alcohol, cleaning the paint from old furniture, and applying shellac to the floors of the rooms. The symptoms consisted in profound involvement of the cerebrum, semi-consciousness, and unintelligible speech; temperature 100°, pulse 108. The pupils were widely dilated and irresponsive to light. The urinary examination was negative. His sight was so seriously affected that he could only count the number of persons in the room and see a hand passed before his face.

Examination of the fundi showed blurring of the disk of the right eye and contraction of the arteries in the left. All the symptoms rapidly cleared up under treatment by elimination and large doses of strychnine, except the sight. Fifteen days after admission the fundus was unchanged, but there was no vision whatever. The pupils continued dilated and irresponsive.

The reporter wisely suggests that, in view of the enormous use of wood alcohol in manufactures, the dangers from inhaling its fumes, as well as its use as a beverage, ought to be widely known.

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